Brand Names

Adhansia XR, Aptensio XR, Concerta, Cotempla XR, Daytrana, Jornay, Metadate CD, Metadate ER, Methylin, QuilliChew ER, Quillivant XR, RELEXXII, Ritalin, Ritalin LA, Ritalin SR

Indication Specific Dosing

For the treatment of attention-deficit hyperactivity disorder (ADHD)

For the treatment of ADHD in persons currently receiving methylphenidate

Oral dosage (extended-release once-daily capsules; Adhansia XR)

Adults 18 to 72 years

25 mg PO once daily in the morning, initially. May increase the dose by 10 to 15 mg/day at intervals of no less than 5 days based on clinical response. Max: 100 mg/day. Although 100 mg was efficacious in short-term controlled trials, dosages above 85 mg/day were associated with a disproportionate increase in the incidence of certain adverse reactions. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years

25 mg PO once daily in the morning, initially. May increase the dose by 10 to 15 mg/day at intervals of no less than 5 days based on clinical response. Max: 85 mg/day. Although 85 mg was efficacious in short-term controlled trials, dosages above 70 mg daily were associated with a disproportionate increase in the incidence of certain adverse reactions. Reduce dose or, if necessary, discontinue

therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Oral dosage (extended-release once-daily capsules; Jornay PM)

Adults 18 to 65 years

20 mg PO once daily in the evening, initially. May increase the dose by 20 mg/day at weekly intervals based on clinical response. Max: 100 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years

20 mg PO once daily in the evening, initially. May increase the dose by 20 mg/day at weekly intervals based on clinical response. Max: 100 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Oral dosage (extended-release once-daily capsules; Ritalin LA)

Children 6 to 12 years weighing more than 50 kg

10 mg PO once daily as extended-release for 5 mg PO twice daily immediate-release; 20 mg PO once daily as extended-release for 10 mg PO twice daily immediate-release; 30 mg PO once daily as extended-release for 15 mg PO twice daily immediate-release; 40 mg PO once daily as extended-release for 20 mg PO twice daily immediate-release; or 60 mg PO once daily as extended-release for 30

mg PO twice daily immediate-release. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 12 years weighing 50 kg or less

10 mg PO once daily as extended-release for 5 mg PO twice daily immediate-release; 20 mg PO once daily as extended-release for 10 mg PO twice daily immediate-release; 30 mg PO once daily as extended-release for 15 mg PO twice daily immediate-release; 40 mg PO once daily as extended-release for 20 mg PO twice daily immediate-release; or 60 mg PO once daily as extended-release for 30 mg PO twice daily immediate-release. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Oral dosage (extended-release once-daily chewable tablets; QuilliChew ER)

Adults 18 to 65 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. However, a maximum dose of 100 mg/day of may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate

products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Adults 18 to 65 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. However, a maximum dose of 100 mg/day of may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children 6 to 17 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis

because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Oral dosage (extended-release once-daily suspension; Quillivant XR)

Adults 18 to 65 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Adults 18 to 65 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Oral dosage (extended-release once-daily tablets; Concerta, Relexxii)

Adults 18 to 65 years weighing more than 50 kg

18 mg PO once daily as extended-release for 5 mg PO 2 or 3 times daily immediate-release; 36 mg PO once daily as extended-release for 10 mg PO 2 or 3 times daily immediate-release; 54 mg PO once daily as extended-release for 15 mg PO 2 or 3 times daily immediate-release; or 72 mg PO once daily as extended-release for 20 mg PO 2 or 3 times daily immediate-release. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 72 mg/day. However, a maximum dose of 108 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Adults 18 to 65 years weighing 50 kg or less

18 mg PO once daily as extended-release for 5 mg PO 2 or 3 times daily immediate-release; 36 mg PO once daily as extended-release for 10 mg PO 2 or 3 times daily immediate-release; 54 mg PO once daily as extended-release for 15 mg PO 2 or 3 times daily immediate-release; or 72 mg PO once daily as extended-release for 20 mg PO 2 or 3 times daily immediate-release. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage

between 18 and 36 mg. Max: 72 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years weighing more than 50 kg

18 mg PO once daily as extended-release for 5 mg PO 2 or 3 times daily immediate-release; 36 mg PO once daily as extended-release for 10 mg PO 2 or 3 times daily immediate-release; 54 mg PO once daily as extended-release for 15 mg PO 2 or 3 times daily immediate-release; or 72 mg PO once daily as extended-release for 20 mg PO 2 or 3 times daily immediate-release. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 72 mg/day. However, a maximum dose of 108 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Children and Adolescents 6 to 17 years weighing 50 kg or less

18 mg PO once daily as extended-release for 5 mg PO 2 or 3 times daily immediate-release; 36 mg PO once daily as extended-release for 10 mg PO 2 or 3 times daily immediate-release; 54 mg PO once daily as extended-release for 15 mg PO 2 or 3 times daily immediate-release; or 72 mg PO once daily as extended-release for 20 mg PO 2 or 3 times daily immediate-release. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 72 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy. Discontinue other methylphenidate products and titrate using the titration schedule. Do not

substitute other methylphenidate products on a milligram-per-milligram basis because of different methylphenidate base compositions and differing pharmacokinetic profiles.

Oral dosage (extended-release tablets; Ritalin SR, Metadate ER, Methylin ER)

Adults 18 to 65 years weighing more than 50 kg

The extended-release (ER) tablets have a duration of action of approximately 8 hours. Use in place of immediate-release (IR) tablets when the 8-hour dosage of these ER tablets corresponds to the titrated 8-hour dosage of the IR tablets. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adults 18 to 65 years weighing 50 kg or less

The extended-release (ER) tablets have a duration of action of approximately 8 hours. Use in place of immediate-release (IR) tablets when the 8-hour dosage of these ER tablets corresponds to the titrated 8-hour dosage of the IR tablets. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing more than 50 kg

The extended-release (ER) tablets have a duration of action of approximately 8 hours. Use in place of immediate-release (IR) tablets when the 8-hour dosage of these ER tablets corresponds to the titrated 8-hour dosage of the IR tablets. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing 50 kg or less

The extended-release (ER) tablets have a duration of action of approximately 8 hours. Use in place of immediate-release (IR) tablets when the 8-hour dosage of these ER tablets corresponds to the titrated 8-hour dosage of the IR tablets. Max:

60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Transdermal dosage

Children and Adolescents 6 to 17 years

10 mg/9 hours transdermally once daily in the morning, initially. May increase the dose to 15 mg/9 hours, then 20 mg/9 hours, and then 30 mg/9 hours at weekly intervals based on clinical response. The patch may be removed earlier than 9 hours if a shorter duration of effect is desired or late day side effects appear. Max: 30 mg/9 hours once daily. In clinical trials, there was no additional benefit of increasing the patch dose from 20 mg/9-hours to 30 mg/9-hours. Follow the titration schedule for persons switching from another formulation of methylphenidate due to differences in bioavailability of the methylphenidate transdermal system compared to other products.

For the treatment of ADHD in persons naive to methylphenidate

Oral dosage (immediate-release)

Adults 18 to 65 years weighing more than 50 kg

20 to 30 mg/day PO in 2 to 3 divided doses. May increase the dose by 5 to 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adults 18 to 65 years weighing 50 kg or less

20 to 30 mg/day PO in 2 to 3 divided doses. May increase the dose by 5 to 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing more than 50 kg

5 mg PO twice daily, initially. May increase the dose by 5 to 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing 50 kg or less

5 mg PO twice daily, initially. May increase the dose by 5 to 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children 3 to 5 years†

1.25 mg PO 3 times daily, initially. May increase the dose gradually based on clinical response. Max: 30 mg/day. The mean optimal total daily dose was 14.2 +/- 8.1 mg (0.7 +/- 0.4 mg/kg/day). In all cases, start treatment with a low dose and titrate upward slowly. Use the lowest effective dose. Higher doses have lead to social withdrawal in some children. Behavior therapy, parental training, and a structured preschool environment are considered first-line treatment for preschool-aged children with ADHD; lack of significant improvement with such modalities may warrant the addition of methylphenidate.

Oral dosage (extended-release once-daily capsules; Adhansia XR)

Adults 18 to 72 years

25 mg PO once daily in the morning, initially. May increase the dose by 10 to 15 mg/day at intervals of no less than 5 days based on clinical response. Max: 100 mg/day. Although 100 mg was efficacious in short-term controlled trials, dosages above 85 mg/day were associated with a disproportionate increase in the incidence of certain adverse reactions. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years

25 mg PO once daily in the morning, initially. May increase the dose by 10 to 15

mg/day at intervals of no less than 5 days based on clinical response. Max: 85 mg/day. Although 85 mg was efficacious in short-term controlled trials, dosages above 70 mg daily were associated with a disproportionate increase in the incidence of certain adverse reactions. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily capsules; Aptensio XR)

Adults weighing more than 50 kg

10 mg PO once daily in the morning, initially. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adults weighing 50 kg or less

10 mg PO once daily in the morning, initially. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing more than 50 kg

10 mg PO once daily in the morning, initially. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing 50 kg or less

10 mg PO once daily in the morning, initially. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed

after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily capsules; Jornay PM)

Adults 18 to 65 years

20 mg PO once daily in the evening, initially. May increase the dose by 20 mg/day at weekly intervals based on clinical response. Max: 100 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years

20 mg PO once daily in the evening, initially. May increase the dose by 20 mg/day at weekly intervals based on clinical response. Max: 100 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily capsules; Metadate CD)

Children and Adolescents 6 to 15 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 15 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily capsules; Ritalin LA)

Children 6 to 12 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. When a lower initial dose is appropriate, start treatment with 10 mg PO once daily. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children 6 to 12 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. When a lower initial dose is appropriate, start treatment with 10 mg PO once daily. May increase the dose by 10 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily chewable tablets; QuilliChew ER)

Adults 18 to 65 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. However, a maximum dose of 100 mg/day of may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adults 18 to 65 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. However, a maximum dose of 100 mg/day of may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10, 15, or 20 mg/day at weekly intervals based on clinical response. The 10 and 15 mg doses can each be achieved by breaking in half the functionally scored 20 and 30 mg tablets, respectively. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily orally disintegrating tablets; Cotempla XR-ODT)

Children and Adolescents 6 to 17 years

17.3 mg PO once daily in the morning, initially. May increase the dose by 8.6 to 17.3 mg/day at weekly intervals based on clinical response. Max: 51.8 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily suspension; Quillivant XR)

Adults 18 to 65 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adults 18 to 65 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing more than 50 kg

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. However, a maximum dose of 100 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children and Adolescents 6 to 17 years weighing 50 kg or less

20 mg PO once daily in the morning, initially. May increase the dose by 10 to 20 mg/day at weekly intervals based on clinical response. Max: 60 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Oral dosage (extended-release once-daily tablets; Concerta, Relexxii)

Adults 18 to 65 years weighing more than 50 kg

18 or 36 mg PO once daily in the morning, initially. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 72 mg/day. However, a maximum dose of 108 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adults 18 to 65 years weighing 50 kg or less

18 or 36 mg PO once daily in the morning, initially. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available

for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 72 mg/day. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adolescents weighing more than 50 kg

18 mg PO once daily in the morning, initially. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 2 mg/kg/day or 72 mg/day, whichever is less. However, a maximum dose of 108 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Adolescents weighing 50 kg or less

18 mg PO once daily in the morning, initially. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 2 mg/kg/day or 72 mg/day, whichever is less. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children 6 to 12 years weighing more than 50 kg

18 mg PO once daily in the morning, initially. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 2 mg/kg/day or 54 mg/day, whichever is less. However, a maximum dose of 108 mg/day may be considered. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Children 6 to 12 years weighing 50 kg or less

18 mg PO once daily in the morning, initially. May increase the dose by 18 mg/day at weekly intervals based on clinical response. A 27 mg tablet is available

for health care providers who wish to utilize a dosage between 18 and 36 mg. Max: 2 mg/kg/day or 54 mg/day, whichever is less. Reduce dose or, if necessary, discontinue therapy if paradoxical aggravation of symptoms or other adverse reactions occur. If improvement is not observed after appropriate dosage adjustment over a 1-month period, discontinue therapy.

Transdermal dosage

Children and Adolescents 6 to 17 years

10 mg/9 hours transdermally once daily in the morning, initially. May increase the dose to 15 mg/9 hours, then 20 mg/9 hours, and then 30 mg/9 hours at weekly intervals based on clinical response. The patch may be removed earlier than 9 hours if a shorter duration of effect is desired or late day side effects appear. Max: 30 mg/9 hours once daily. In clinical trials, there was no additional benefit of increasing the patch dose from 20 mg/9-hours to 30 mg/9-hours.

For the treatment of narcolepsy

Oral dosage (immediate-release)

Adults

20 to 60 mg/day PO in 2 to 3 divided doses. Adjust dose based on clinical response and tolerability. Usual dose: 20 to 30 mg/day. Max: 60 mg/day.

Children and Adolescents 6 to 17 years

5 mg PO twice daily, initially. May increase the dose by 5 to 10 mg/day at weekly intervals based on clinical response and tolerability. Max: 60 mg/day.

Oral dosage (extended-release†)

Children and Adolescents 6 to 17 years

18 to 60 mg PO once daily.

Transdermal dosage†

Children and Adolescents 6 to 17 years

10 to 30 mg/9 hours transdermally once daily.

For the treatment of major depression† or post-stroke depression refractory to other therapies

Oral dose (immediate-release tablets)

Adults

Initially, 2.5 mg PO twice daily administered in the morning and at noon; increase by 2.5—5 mg PO every 2 or 3 days as tolerated, until the desired response is achieved. Roughly 50% of patients appear to respond to treatment.

Geriatric

Initially, 2.5 mg PO twice daily administered in the morning and at noon; increase by 2.5—5 mg PO every 2 or 3 days as tolerated, until the desired response is achieved. Dosage in elderly patients with post-stroke depression has ranged from 15—40 mg/day PO after dosage titration for a mean of 15 days. Roughly 50% of patients appear to respond to treatment.

For the treatment of amphetamine-type stimulant use disorder†

Oral dosage (extended-release solid formulations for once-daily administration, e.g., Concerta, Metadate CD, Relexxii, Ritalin LA)

Adults

Usual dosage range from studies: 60 to 90 mg/day. Some patients may require doses at or above the maximum FDA-approved ADHD dose (e.g., 180 mg/day) based on some studies to effectively reduce usage of stimulants such as amphetamine or methamphetamine (low certainty, conditional recommendation). Long-acting methylphenidate formulations may be particularly beneficial for patients with moderate or high frequency of amphetamine-type stimulant use (i.e., 10 or more days per month) or those with comorbid ADHD. One guideline suggests that the use of psychostimulants for this indication be limited to specialists who are board certified in addiction medicine, addiction psychiatry, or commensurate training and competency.

Contraindications And Precaution

Drug Interactions

The coadministration of certain medications may lead to harm and require avoidance or therapy modification; review all drug interactions prior to concomitant use of other medications.

Hypersensitivity

This medication is contraindicated in patients with a history of hypersensitivity to it or any of its components. Cross-sensitivity with dexmethylphenidate should be expected. Life-threatening hypersensitivity reactions, including angioedema and anaphylaxis, have been reported during methylphenidate administration. The use of transdermal methylphenidate may lead to contact sensitization. If contact sensitization is suspected, the methylphenidate patch should be discontinued. Patients who have previously developed contact dermatitis with transdermal methylphenidate may also be sensitized to oral methylphenidate and should be initiated on oral therapy under close supervision. After initial development of contact dermatitis from the methylphenidate patch, re-exposure to the drug by other routes of administration may result in systemic sensitization or other systemic reactions. Symptoms may include a flare-up of previous dermatitis, generalized skin eruptions to previously unaffected skin, headache, fever, malaise, arthralgia, diarrhea, or vomiting. Some patients who develop sensitization to the patch may not be able to use the oral products. Patients should alternate hip application sites each day to help prevent sensitization.

tics, Tourette's syndrome

CNS stimulants, including methylphenidate products, have been associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette syndrome has also been reported. Prior to initiating any methylphenidate product, carefully assess family history and clinically evaluate individuals for motor or verbal tics or Tourette syndrome. Regularly monitor methylphenidate-treated individuals for the emergence or worsening of tics or Tourette syndrome and discontinue treatment if clinically appropriate.

glucose-galactose malabsorption, hereditary fructose intolerance, sucrase-isomaltase deficiency

The Metadate CD products (and approved CD generics) contain sucrose. The manufacturers consider these products contraindicated in patients with hereditary fructose intolerance, glucose-galactose malabsorption, and sucrase-isomaltase deficiency.

mood disorder, psychotic disorder, suicidal ideation

CNS stimulants should be used with caution in those with bipolar disorder or a pre-existing psychotic disorder (e.g., schizophrenia). CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in individuals with pre-existing psychosis. These medications can also induce mania or a mixed episode in individuals with bipolar disorder. Prior to initiating treatment with methylphenidate, screen

individuals for risk factors for bipolar disorder or developing an episode of mania (e.g., mood disorder, comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, or depression). At recommended doses, CNS stimulants may also cause psychotic or manic symptoms (such as hallucinations, delusions, or mania) in individuals without a prior history of psychosis or mania. Advise individuals and their caregivers to promptly report suicidal ideation or any changes in mood or behavior and consider discontinuing treatment if these symptoms occur.

glaucoma

Methylphenidate should be used cautiously in individuals at risk of glaucoma. Increased intraocular pressure (IOP) and angle closure glaucoma have been reported in association with methylphenidate treatment. While the mechanism is not clear, methylphenidate-treated individuals considered at risk for acute angle closure glaucoma (e.g. individuals with significant hyperopia) should be evaluated by an ophthalmologist. Individuals with a history of open-angle glaucoma or abnormally increased IOP should only receive methylphenidate if the benefit of treatment outweighs the risk. These individuals should be monitored closely for changes in vision. Visual disturbance has been reported with the use of methylphenidate and may present as difficulties with accommodation and blurring of vision.

substance abuse disorder

Central nervous system (CNS) stimulants, such as methylphenidate, have a high potential for abuse and misuse, which can lead to the development of a substance abuse disorder, including addiction. Caution is recommended in individuals with a known history of substance abuse, including alcoholism. Assess each individual's risk for abuse, misuse, or addiction before prescribing a CNS stimulant, and monitor for the development of these behaviors or conditions throughout treatment. Children and adolescents with attention-deficit hyperactivity disorder (ADHD) are more prone to substance abuse compared to those without ADHD, and those with co-occurring mental health conditions (e.g., depression, disruptive behavior disorders) are at even greater risk; however, appropriate treatment of ADHD with medication and behavior therapy may reduce the risk of developing a substance abuse disorder. Prescribing and dispensing the smallest appropriate quantity may help to minimize abuse, misuse, and overdosage. CNS stimulants can be diverted for non-medical use into illicit channels or distribution. The most common source of non-medical use is sharing from family or friends with misuse of the individual's own prescription or obtaining from illicit channels occurring less frequently. Sharing of CNS stimulant medications can lead to substance abuse disorder and addiction in those they are shared with. Misuse and abuse of CNS stimulants can result in potential for overdose or poisoning and death; the risk is

increased with higher doses or unapproved methods of administration, such as snorting or injection. Educate individuals and their families about these risks, proper storage, and proper disposal of any unused medication. Misuse or abuse may cause increased heart rate, respiratory rate, or blood pressure; sweating; dilated pupils; hyperactivity; restlessness; insomnia; decreased appetite; loss of coordination; tremors; flushed skin; vomiting; and/or abdominal pain. Anxiety, psychosis, hostility, aggression, and suicidal or homicidal ideation have also been observed with stimulant abuse or misuse.

cardiac disease, family history of sudden cardiac death

Sudden death has been reported in individuals with structural cardiac abnormalities or other serious cardiac disease who were treated with CNS stimulants at the recommended ADHD dosages. Avoid use of CNS stimulants in individuals with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmias, coronary artery disease, or other serious cardiac disease. Prior to initiating any CNS stimulant, carefully assess the individual for the presence of cardiac disease (i.e., perform a careful patient history, assess for any family history of sudden death or ventricular arrhythmia, and complete a physical exam) and counsel individuals to report symptoms of cardiac disease (i.e., exertional chest pain, unexplained syncope) immediately. Although it is reasonable for a health care provider to obtain an ECG as part of the cardiovascular evaluation, it is not mandatory. Treatment with stimulant products should not be withheld because an ECG is not performed. However, any patient with significant findings on physical examination, ECG, or from patient or family history (such as known congenital heart disease, structural heart disease, arrhythmias, or a family history of sudden cardiac death in members younger than 35 years of age) should be referred for consultation with a pediatric cardiologist prior to starting the stimulant medication. Overall, studies have not shown an association between the use of ADHD medications and adverse cardiovascular events; however, long-term cardiovascular risks associated with ADHD medications are unknown. CNS stimulant medications, including methylphenidate, can cause an increase in blood pressure (mean increase approximately 2 to 4 mmHg) and heart rate (mean increase approximately 3 to 6 beats per minute). Some individuals may have larger increases. Monitor all individuals receiving methylphenidate for hypertension and tachycardia. Careful monitoring should be performed after initiation of stimulant medications; if any abnormal findings or arrhythmias are diagnosed during treatment, consider discontinuation of the stimulant.

children

Extended-release methylphenidate is not recommended for use in children younger than 6 years due to higher medication exposure and increased adverse reactions. An FDA analysis reported children younger than 6 years receiving extended-release

stimulants have higher adverse reaction rates, particularly significant weight loss, compared to older children on the same dose. For children younger than 6 years who experience weight loss or other adverse reactions while receiving extended-release stimulants, consider discontinuing the medication or switching to an alternative, such as an immediate-release stimulant. Monitor growth and development and provide necessary interventions to minimize weight loss.

cystic fibrosis, GI obstruction, Meckel diverticulum, peritonitis, short bowel syndrome

There is a potential for Concerta or Relexxii tablets to cause GI obstruction in susceptible individuals. The Concerta and Relexxii extended-release tablets are nondeformable and do not change shape when passing through the GI tract. Use with caution in individuals who have a history of severe GI narrowing, such as those individuals with inflammatory bowel disease, short bowel syndrome, history of peritonitis, cystic fibrosis, chronic intestinal pseudo-obstruction, or Meckel diverticulum. Individuals with dysphagia, esophageal motility disorders, or esophageal stricture may not be able to swallow extended-release methylphenidate dosage forms whole and may be at risk for GI obstruction.

peripheral vasoconstriction or ischemia

Stimulant medications are associated with peripheral vasoconstriction or ischemia, including Raynaud phenomenon. Worsening of peripheral vascular disease is possible. Effects on circulation have been observed with therapeutic doses at different times throughout therapy in all age groups. Signs and symptoms are usually intermittent and mild, and generally improve after reduction in dose or discontinuation of the drug. However, very rare sequelae include digital skin ulcer and/or soft tissue breakdown. Carefully monitor all individuals for digital changes during treatment with stimulant medications, especially those with pre-existing circulation problems. Instruct individuals to seek immediate medical attention if any new digital numbness, pain, skin discoloration, or temperature sensitivity occur, or if unexplained wounds appear on their fingers or toes. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain individuals.

conditions contributing to an elevated core body temperature

Use of the methylphenidate patch does not need to be interrupted during bathing or hot weather, but conditions contributing to an elevated core body temperature, such as prolonged exposure to an external heat source (e.g., heating pad, hair dryer, hot tub, sauna, or electric blanket) should be avoided in order to avoid potential adverse effects

from increased methylphenidate exposure. There is a potential for temperature-dependent increases in methylphenidate release of greater than 2-fold from the patch when there is extreme ambient temperature increase at the site of application.

vitiligo

Chemical leukoderma, skin hypopigmentation due to repeated exposure to specific chemical compounds, may occur with use of the methylphenidate patch; individuals with a personal and/or family history of vitiligo may be more at risk. This condition is not physically harmful, but is disfiguring and is thought to be irreversible, which may cause emotional distress. Advise individuals and caregivers to monitor for new areas of skin discoloration, especially under the drug patch, and report any changes to their health care professional immediately. If chemical leukoderma occurs, discontinue the patch and consider alternative treatment options. Chemical leukoderma can mimic the appearance of vitiligo. Areas of skin color loss described have ranged up to 8 inches in diameter and were mostly limited to areas where the patch was rotated; however, a few individuals have reported discoloration on parts of the body where the patch was never applied. Time to onset has ranged from 2 months to 4 years after patch initiation.]

pregnancy

Published studies and postmarketing reports on the use of methylphenidate during pregnancy have not identified a drug-associated risk of major birth defects, miscarriage, or adverse pregnancy outcomes. However, there may be risks to the fetus associated with the use of CNS stimulants during pregnancy. CNS stimulants can cause vasoconstriction, and thereby decrease placental perfusion. Several cohort studies have reported an increased risk of spontaneous abortion, pre-eclampsia, preterm birth, and perinatal complications associated with the use of methylphenidate during pregnancy, while other studies have also shown an increase in these complications in patients with ADHD not taking medication. Methylphenidate has also been associated with a small increased risk of cardiac malformations in some studies, while other studies have shown no increase in risk after controlling for concomitant medications and medical comorbidities. No fetal and/or neonatal adverse reactions have been reported with the use of therapeutic doses of methylphenidate during pregnancy; however, premature delivery and low birth weight infants have been reported in amphetamine-dependent pregnant patients. Care teams are encouraged to register patients in the National Pregnancy Registry for ADHD Medications at https://womensmentalhealth.org/research/postpregnancy/ad-hd-medications/ or by calling 1-866-961-2388. Non-prescribed use of stimulants during pregnancy is not recommended because of associated maternal and fetal harm. Neonates of patients

with stimulant use disorder may experience withdrawal after delivery, which may present as feeding difficulty, irritability, agitation, and excessive drowsiness.

phenylketonuria

Methylphenidate chewable tablets (e.g., Methylin, QuilliChew ER) contain aspartame. Phenylalanine is a component of aspartame and can be harmful to individuals with phenylketonuria (PKU). Before prescribing these formulations in individuals with PKU, consider the combined daily amount of phenylalanine from all sources.

breast-feeding

Use methylphenidate with caution during breast-feeding. If methylphenidate is required in the lactating individual, its use is not a reason to discontinue breast-feeding. Methylphenidate is present in human milk. Based on data from milk samples from 7 lactating patients, the relative infant dose is 0.16% to 0.7% and the milk-to-plasma ratio is 1.1 to 2.7. There have been no reports of adverse effects on the breastfed child or effects on milk production. If methylphenidate is taken during lactation, monitor the breastfed child for adverse reactions, including decreased appetite, reduced weight gain, insomnia, and agitation. The effect of stimulant medication exposure via human milk on long-term neurological development is unknown. Consider the benefits of breast-feeding, the patient's clinical need for treatment, and any potential adverse effects on the breastfed child from the medication or from the patient's underlying medical condition.

Pregnancy And Lactation

Published studies and postmarketing reports on the use of methylphenidate during pregnancy have not identified a drug-associated risk of major birth defects, miscarriage, or adverse pregnancy outcomes. However, there may be risks to the fetus associated with the use of CNS stimulants during pregnancy. CNS stimulants can cause vasoconstriction, and thereby decrease placental perfusion. Several cohort studies have reported an increased risk of spontaneous abortion, pre-eclampsia, preterm birth, and perinatal complications associated with the use of methylphenidate during pregnancy, while other studies have also shown an increase in these complications in patients with ADHD not taking medication. Methylphenidate has also been associated with a small increased risk of cardiac malformations in some studies, while other studies have shown no increase in risk after controlling for concomitant medications and medical comorbidities. No fetal and/or neonatal adverse reactions have been reported with the use of therapeutic doses of methylphenidate during pregnancy; however, premature

delivery and low birth weight infants have been reported in amphetamine-dependent pregnant patients. Care teams are encouraged to register patients in the National Pregnancy Registry for ADHD Medications at https://womensmentalhealth.org/research/postpregnancy/ad-hd-medications/ or by calling 1-866-961-2388. Non-prescribed use of stimulants during pregnancy is not recommended because of associated maternal and fetal harm. Neonates of patients with stimulant use disorder may experience withdrawal after delivery, which may present as feeding difficulty, irritability, agitation, and excessive drowsiness.

Interactions

Acarbose: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Acebutolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of

methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) If concomitant use of dihydrocodeine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; Caffeine; Pyrilamine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Acetaminophen; Chlorpheniramine; Phenylephrine : (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Acetaminophen; Codeine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; Dextromethorphan; guaiFENesin; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-

prescription medications such as pseudoephedrine and phenylephrine.
Acetaminophen; Dextromethorphan; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Acetaminophen; guaiFENesin; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Acetaminophen; HYDROcodone: (Moderate) If concomitant use of hydrocodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; oxyCODONE: (Moderate) If concomitant use of oxycodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
ALFentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering alfentanil with methylphenidate derivatives. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Aliskiren: (Moderate) Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including aliskiren. Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidates and antihypertensive agents,

particularly during initial coadministration and after dosage increases of methylphenidate derivatives.
Aliskiren; hydroCHLOROthiazide, HCTZ: (Moderate) Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including aliskiren. Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidates and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Alogliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Alogliptin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Alogliptin; Pioglitazone: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta-

receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Alpha-blockers: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate. Methylphenidates can reduce the hypotensive effect of antihypertensive agents such as alpha-blockers.
Alpha-glucosidase Inhibitors: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Amantadine: (Moderate) Use of amantadine with methylphenidate derivatives, which are CNS stimulants, requires careful observation. Coadministration may increase the risk of stimulant effects, such as nervousness, irritability, insomnia, tremor, seizures, or cardiac arrhythmias.
Ambrisentan: (Moderate) Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents. Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidates and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives.
Amifampridine: (Major) Carefully consider the need for concomitant treatment with methylphenidate derivatives and amifampridine, as coadministration may increase the risk of seizures. If coadministration occurs, closely monitor patients for seizure activity. Seizures have been observed in patients without a history of seizures taking amifampridine at recommended doses. Methylphenidate derivatives may increase the risk of seizures.
aMILoride: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
aMILoride; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing

diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Amitriptyline: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
amLODIPine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
amLODIPine; Atorvastatin: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
amLODIPine; Benazepril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
amLODIPine; Celecoxib: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
amLODIPine; Olmesartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.

(Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
amLODIPine; Valsartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Amoxapine: (Moderate) Methylphenidate derivatives and amoxapine may lower the seizure threshold; therefore, caution is particularly advisable when this combination is administered to patients susceptible to seizures. In addition, methylphenidate is thought to exert some of its beneficial effects through dopamine re-uptake blockade while amoxapine has central dopamine antagonist properties. In theory, the therapeutic effects of either agent may be reduced.
Angiotensin II receptor antagonists: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Angiotensin II: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.

Angiotensin-converting enzyme inhibitors: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Apomorphine: (Moderate) Increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and dopamine agonists such as pergolide, pramipexole, apomorphine, and ropinirole. Dopaminergic side effects, such as nausea, loss of appetite, weight loss, insomnia, tremor, nervousness, or changes in mood or behavior, are possible.
Armodafinil: (Major) The use of armodafinil with other psychostimulants, including methylphenidate derivatives, has not been studied. Patients receiving combination therapy of armodafinil with other psychostimulants should be closely observed for signs of nervousness, irritability, insomnia, arrhythmias, or other stimulant-related side effects.
Articaine; EPINEPHrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Aspirin, ASA; Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary

supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Aspirin, ASA; oxyCODONE: (Moderate) If concomitant use of oxycodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Atenolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Atenolol; Chlorthalidone: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Azilsartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Azilsartan; Chlorthalidone: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Benazepril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.

Benazepril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Moderate) Theoretically, concurrent use of methylene blue and methylphenidate derivatives may increase the risk of serotonin syndrome. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and methylphenidate increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by the rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Beta-blockers: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Betaxolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bethanechol: (Moderate) Bethanechol offsets the effects of sympathomimetics at sites where sympathomimetic and cholinergic receptors have opposite effects.
Bexagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose

concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Bisoprolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bretylium: (Moderate) Monitor blood pressure and heart rate closely when sympathomimetics are administered with bretylium. The pressor and arrhythmogenic effects of catecholamines are enhanced by bretylium.
Brimonidine; Timolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bromocriptine: (Moderate) Increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and dopamine agonists such as bromocriptine. Dopaminergic side effects, such as nausea, loss of appetite, weight loss, insomnia, tremor, nervousness, or changes in mood or behavior, are possible.
Brompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Brompheniramine; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications

such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Bumetanide: (Moderate) Monitor blood pressure during concomitant loop diuretic and methylphenidate use; a loop diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
BUPivacaine; EPINEPHrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Buprenorphine: (Moderate) If concomitant use of buprenorphine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Buprenorphine; Naloxone: (Moderate) If concomitant use of buprenorphine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
buPROPion: (Moderate) Use extreme caution when coadministering bupropion with other drugs that lower the seizure threshold, such as stimulants including methylphenidate. Use low initial doses of bupropion and increase the dose gradually.
buPROPion; Naltrexone: (Moderate) Use extreme caution when coadministering bupropion with other drugs that lower the seizure threshold, such as stimulants including methylphenidate. Use low initial doses of bupropion and increase the dose gradually.
Butalbital; Acetaminophen; Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of

methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Caffeine; Sodium Benzoate: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute

to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Calcium, Magnesium, Potassium, Sodium Oxybates: (Moderate) The stimulant effects of methylphenidate derivatives can be additive when used concurrently with other psychostimulants, such as sodium oxybate. The combination may increase the incidence of side effects; if these combinations cannot be avoided the patient should be closely observed for signs of nervousness, irritability, insomnia, arrhythmias, or other stimulant-related problems. Sodium oxybate has the potential to induce seizures; it has been speculated that this effect may be mediated through the action of sodium oxybate at GABA receptors. Although convulsant effects occur primarily at high dosages, sodium oxybate should be used cautiously with psychostimulants that are known to lower seizure threshold. Note that CNS stimulants, including methylphenidate, are frequently used in the treatment of narcolepsy, and clinical trials involving the use of psychostimulants with sodium oxybate have not found the combinations to be unsafe. Pharmacodynamic interactions cannot be ruled out, however.
Calcium-channel blockers: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Canagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Canagliflozin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Candesartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate

may decrease the effectiveness of drugs used to treat hypertension.
Candesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Captopril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Captopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
carBAMazepine: (Minor) Psychostimulants, such as methylphenidate and its derivatives, may lower the seizure threshold, thereby reducing the efficacy of anticonvulsants such as carbamazepine. There are rare case reports of reduced methylphenidate concentrations occurring during the use of carbamazepine concurrently. The mechanism of the interaction is not clear as methylphenidate is metabolized primarily to ritalinic acid by nonmicrosomal hydrolytic esterases that are widely distributed throughout the body. Interactions with other potent enzyme inducers have not been reported. Monitor for any changes in therapeutic effectiveness of either drug.
Carbidopa; Levodopa; Entacapone: (Minor) Due to their pharmacologic actions, it is thought that increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and COMT inhibitors. Be alert for any dopamine-related side effects such as nausea, reduced appetite, tremor, or changes in moods or behaviors.
Carteolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Carvedilol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be

necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Celecoxib; Tramadol: (Moderate) Concurrent use of tramadol and methylphenidate derivatives might increase the risk for serotonin syndrome. If concomitant use is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome. There are also postmarketing reports of serotonin syndrome during concurrent use of methylphenidate or methylphenidate derivatives with other serotonergic medications.
chlordiazePOXIDE; Amitriptyline: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Chlorothiazide: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Chlorpheniramine; Codeine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Chlorpheniramine; HYDROcodone: (Moderate) If concomitant use of hydrocodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Chlorpheniramine; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and

endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Chlorthalidone: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Citalopram: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Clevidipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
clomiPRAMINE: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
cloNIDine: (Moderate) Monitor blood pressure during concomitant clonidine and methylphenidate use; a clonidine dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Cocaine: (Major) Avoid concomitant use of additional vasoconstrictor agents with cocaine. If unavoidable, prolonged vital sign and ECG monitoring may be required. Myocardial ischemia, myocardial infarction, and ventricular arrhythmias have been reported after concomitant administration of topical intranasal cocaine and vasoconstrictor agents during nasal and sinus surgery. The risk for nervousness, irritability, convulsions, and other cardiac arrhythmias may increase during coadministration.
Codeine: (Moderate) If concomitant use of codeine and methylphenidate or its

derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; Dexbrompheniramine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; guaiFENesin: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; Phenylephrine; Promethazine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome. (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Codeine; Promethazine: (Moderate) If concomitant use of codeine and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
COMT inhibitors: (Minor) Due to their pharmacologic actions, it is thought that increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and COMT inhibitors. Be alert for any

dopamine-related side effects such as nausea, reduced appetite, tremor, or changes in moods or behaviors.
Dapagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Dapagliflozin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Dapagliflozin; sAXagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Desflurane: (Major) Avoid the use of methylphenidate or its derivatives in patients being treated with halogenated anesthetics (e.g., enflurane, halothane, isoflurane, and methoxyflurane) on the day of surgery. The use of Metadate CD is contraindicated on

the day of surgery. Halogenated anesthetics may sensitize the cardiovascular system to the effects of methylphenidate increasing the risk of sudden blood pressure and heart rate increase during surgery.
Desipramine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Desvenlafaxine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and serotonin norepinephrine reuptake inhibitors (SNRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. There is also a case of a neuroleptic malignant syndrome-like reaction occurring in a child on chronic methylphenidate therapy after ingesting methylphenidate with an SNRI. It is unclear if the reaction was the result of a drug interaction. Monitor patients for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Dexbrompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Dextromethorphan; buPROPion: (Moderate) Use extreme caution when coadministering bupropion with other drugs that lower the seizure threshold, such as stimulants including methylphenidate. Use low initial doses of bupropion and increase the dose gradually.
Dextromethorphan; diphenhydrAMINE; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Dextromethorphan; guaiFENesin; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription

medications such as pseudoephedrine and phenylephrine.
Diazoxide: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
dilTIAZem: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Dipeptidyl Peptidase-4 Inhibitors: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
diphenhydrAMINE; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
dopamine agonists: (Moderate) Increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and dopamine agonists such as pergolide, pramipexole, apomorphine, and ropinirole. Dopaminergic side effects, such as nausea, loss of appetite, weight loss, insomnia, tremor, nervousness, or changes in mood or behavior, are possible.
DOPamine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Dorzolamide; Timolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage

adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Doxazosin: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate. Methylphenidates can reduce the hypotensive effect of antihypertensive agents such as alpha-blockers.
Doxepin: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
droNABinol: (Moderate) Concurrent use of dronabinol, THC with sympathomimetics may result in additive hypertension, tachycardia, and possibly cardiotoxicity. Dronabinol, THC has been associated with occasional hypotension, hypertension, syncope, and tachycardia. In a study of 7 adult males, combinations of IV cocaine and smoked marijuana, 1 g marijuana cigarette, 0 to 2.7% delta-9-THC, increased the heart rate above levels seen with either agent alone, with increases plateauing at 50 bpm.
Droxidopa: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Dulaglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
DULoxetine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and serotonin norepinephrine reuptake inhibitors (SNRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. There is also a case of a neuroleptic malignant syndrome-like reaction occurring in a child on chronic

methylphenidate therapy after ingesting methylphenidate with an SNRI. It is unclear if the reaction was the result of a drug interaction. Monitor patients for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Empagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Empagliflozin; Linagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Empagliflozin; Linagliptin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss

of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Empagliflozin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Enalapril, Enalaprilat: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Enalapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Entacapone: (Minor) Due to their pharmacologic actions, it is thought that increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and COMT inhibitors. Be alert for any dopamine-related side effects such as nausea, reduced appetite, tremor, or changes in moods or behaviors.
ePHEDrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as

pseudoephedrine and phenylephrine.
ePHEDrine; guaiFENesin: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
EPINEPHrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Eplerenone: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as eplerenone.
Epoprostenol: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Ergotamine; Caffeine: (Moderate) Caffeine is a CNS stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Avoid excessive caffeine intake during use of methylphenidate or its derivatives. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Ertugliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic

medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Ertugliflozin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Ertugliflozin; SITagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Escitalopram: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Esketamine: (Major) Closely monitor blood pressure during concomitant use of

esketamine and methylphenidate or its derivatives. Coadministration of psychostimulants, such as methylphenidates, with esketamine may increase blood pressure, including the possibility of hypertensive crisis.
Esmolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Ethacrynic Acid: (Moderate) Monitor blood pressure during concomitant loop diuretic and methylphenidate use; a loop diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Ethanol: (Major) Alcohol consumption should be avoided during treatment with certain extended-release (ER) dosage forms of methylphenidate (e.g., Ritalin LA, Metadate CD). Results from an in vitro study showed that at an alcohol concentration of 40%, there was a 98% release of extended-release methylphenidate (Ritalin LA) from the 40 mg capsule in the first hour after administration. In addition, concurrent use with alcohol may exacerbate the CNS-related adverse effects of methylphenidate.
Ethiodized Oil: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Exenatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Felodipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Fenfluramine: (Moderate) Use fenfluramine and methylphenidate derivatives with caution due to an increased risk of serotonin syndrome. Monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Fenoldopam: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired

antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
fentaNYL: (Moderate) If concomitant use of fentanyl and methylphenidate or its derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
FLUoxetine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Fluticasone; Umeclidinium; Vilanterol: (Moderate) Administer sympathomimetics with caution with beta-agonists such as vilanterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
Fluticasone; Vilanterol: (Moderate) Administer sympathomimetics with caution with beta-agonists such as vilanterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
fluvoxaMINE: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Fosinopril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.

Fosinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Fosphenytoin: (Moderate) Monitor phenytoin concentrations during concomitant therapy with fosphenytoin and methylphenidate; a fosphenytoin dosage decrease may be necessary. Methylphenidate may inhibit the metabolism of fosphenytoin.
Furosemide: (Moderate) Monitor blood pressure during concomitant loop diuretic and methylphenidate use; a loop diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Gepirone: (Moderate) Monitor for serotonin syndrome if concomitant use of gepirone and methylphenidate is necessary. Both medications affect the serotonergic neurotransmitter system; concomitant use increases the risk for serotonin syndrome.
Glimepiride: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glipiZIDE: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glipiZIDE; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas.

Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glyBURIDE: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas.
Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glyBURIDE; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas.
Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
guaiFENesin; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
guanFACINE: (Moderate) Psychostimulants, such as methylphenidate and its derivatives, may increase blood pressure and reduce the antihypertensive effects of antihypertensive agents, such as guanfacine. Monitor blood pressure and heart rate periodically when prescribed together. Guanfacine may be used adjunctively to methylphenidate and its derivatives in the treatment of attention deficit hyperactivity disorder (ADHD). Pharmacokinetic studies reveal that guanfacine does not influence methylphenidate pharmacokinetics and methylphenidate does not affect guanfacine pharmacokinetics. No dosage adjustments are required when used together. Patients should be monitored for heart rate, blood pressure, and for sedation during ADHD treatment.

Halogenated Anesthetics: (Major) Avoid the use of methylphenidate or its derivatives in patients being treated with halogenated anesthetics (e.g., enflurane, halothane, isoflurane, and methoxyflurane) on the day of surgery. The use of Metadate CD is contraindicated on the day of surgery. Halogenated anesthetics may sensitize the cardiovascular system to the effects of methylphenidate increasing the risk of sudden blood pressure and heart rate increase during surgery.
Homatropine; HYDROcodone: (Moderate) If concomitant use of hydrocodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
hydrALAZINE: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
hydrALAZINE; Isosorbide Dinitrate, ISDN: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present. (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
hydroCHLOROthiazide, HCTZ; Moexipril: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
HYDROcodone: (Moderate) If concomitant use of hydrocodone and methylphenidate

derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
HYDROcodone; Ibuprofen: (Moderate) If concomitant use of hydrocodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
HYDROmorphone: (Moderate) If concomitant use of hydromorphone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Moderate) Theoretically, concurrent use of methylene blue and methylphenidate derivatives may increase the risk of serotonin syndrome. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and methylphenidate increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by the rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Iloprost: (Major) Avoid use of sympathomimetic agents with iloprost. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including iloprost. Sympathomimetics can increase blood pressure, increase heart rate, and may cause

vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Imipramine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Incretin Mimetics: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Indacaterol; Glycopyrrolate: (Moderate) Administer sympathomimetics with caution with beta-agonists such as indacaterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
Indapamide: (Moderate) Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as indapamide. Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives.
Insulin Aspart: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for

diabetes.
Insulin Aspart; Insulin Aspart Protamine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Degludec: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Degludec; Liraglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Detemir: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic

glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Glargine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Glargine; Lixisenatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Glulisine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.

Insulin Lispro: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Lispro; Insulin Lispro Protamine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin, Inhaled: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulins: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Iobenguane I 131: (Major) Discontinue sympathomimetics for at least 5 half-lives before the administration of the dosimetry dose or a therapeutic dose of iobenguane I-131. Do not restart sympathomimetics until at least 7 days after each iobenguane I-131 dose. Drugs that reduce catecholamine uptake or deplete catecholamine stores, such as

sympathomimetics, may interfere with iobenguane I-131 uptake into cells and interfere with dosimetry calculations resulting in altered iobenguane I-131 efficacy.
Iodixanol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Ioflupane I 123: (Major) Hold methylphenidate and methylphenidate derivatives for 7 days, or at least 5 medication half-lives, prior to performing dopamine transporter (DAT) imaging with radiolabeled ioflupane. Methylphenidate binds to the dopamine transporter which may interfere with striatal tracer binding and increase the risk for a false-positive scan.
Iohexol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Iomeprol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Iopamidol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Iopromide: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Ioversol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Irbesartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to

treat hypertension.
Isocarboxazid: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
Isoflurane: (Major) Avoid the use of methylphenidate or its derivatives in patients being treated with halogenated anesthetics (e.g., enflurane, halothane, isoflurane, and methoxyflurane) on the day of surgery. The use of Metadate CD is contraindicated on the day of surgery. Halogenated anesthetics may sensitize the cardiovascular system to the effects of methylphenidate increasing the risk of sudden blood pressure and heart rate increase during surgery.
Isophane Insulin (NPH): (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Isosorbide Dinitrate, ISDN: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Isosorbide Mononitrate: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Isosulfan Blue: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Isradipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Ketamine: (Moderate) Closely monitor vital signs when ketamine and methylphenidate derivatives are coadministered; consider dose adjustment individualized to the patient's

clinical situation. Methylphenidate derivatives may enhance the sympathomimetic effects of ketamine.
Labetalol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Landiolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Lasmiditan: (Moderate) Serotonin syndrome may occur during coadministration of lasmiditan and methylphenidate derivatives. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Levamlodipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Levobunolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Levomilnacipran: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and serotonin norepinephrine reuptake inhibitors (SNRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. There is also a case of a neuroleptic malignant syndrome-like reaction occurring in a child on chronic methylphenidate therapy after ingesting methylphenidate with an SNRI. It is unclear if the reaction was the result of a drug interaction. Monitor patients for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Levorphanol: (Moderate) If concomitant use of levorphanol and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Levothyroxine: (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid

hormone.
Levothyroxine; Liothyronine (Porcine): (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Lidocaine; EPINEPHrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Linagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Linagliptin; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Linezolid: (Major) Psychostimulants, such as methylphenidate derivatives, exhibit sympathomimetic actions and should be avoided with other drugs, such as linezolid, that enhance the pressor response of sympathomimetic agents. A clinically significant rise in systolic blood pressure is possible. In addition, serotonin syndrome has been reported during the concurrent use of linezolid, a non-selective monoamine oxidase inhibitor (MAOI), and medications that enhance central serotonergic activity. Monoamine oxidase (MAO) is the enzyme responsible for the degradation of norepinephrine, dopamine, and serotonin. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Patients receiving this combination should be monitored for the emergence of serotonin

syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Liothyronine: (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Liraglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Lisinopril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Lithium: (Moderate) Monitor for serotonin syndrome, particularly during lithium initiation, during concomitant methylphenidate use. If serotonin syndrome occurs, consider discontinuation of lithium and/or methylphenidate.
Lixisenatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for

diabetes.
Loop diuretics: (Moderate) Monitor blood pressure during concomitant loop diuretic and methylphenidate use; a loop diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Losartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Losartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Macitentan: (Major) Avoid use of sympathomimetic agents with macitentan. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including macitentan. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Macitentan; Tadalafil: (Major) Avoid use of sympathomimetic agents with macitentan. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including macitentan. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Maprotiline: (Moderate) Use maprotiline and sympathomimetics together with caution and close clinical monitoring. Regularly assess blood pressure, heart rate, the efficacy of treatment, and the emergence of sympathomimetic/adrenergic adverse events. Carefully adjust dosages as clinically indicated. Maprotiline has pharmacologic activity similar to tricyclic antidepressant agents and may cause additive sympathomimetic

effects when combined with agents with adrenergic/sympathomimetic activity.
Mecamylamine: (Major) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by mecamylamine. Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed.
Meglitinides: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Meperidine: (Moderate) If concomitant use of meperidine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
metFORMIN; sAXagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
metFORMIN; SITagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Methadone: (Moderate) If concomitant use of methadone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin

syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Moderate) Theoretically, concurrent use of methylene blue and methylphenidate derivatives may increase the risk of serotonin syndrome. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and methylphenidate increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by the rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Methyldopa: (Moderate) Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including methyldopa. Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives.
Methylene Blue: (Moderate) Theoretically, concurrent use of methylene blue and methylphenidate derivatives may increase the risk of serotonin syndrome. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and methylphenidate increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene

blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by the rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Metoclopramide: (Moderate) In theory, metoclopramide and methylphenidate derivatives may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Patients receiving this combination should be monitored for loss of effectiveness of either agent. Methylphenidate derivatives blocks central dopamine reuptake, which increases central dopaminergic functioning, while metoclopramide is a dopamine antagonist.
metOLazone: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Metoprolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Midodrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Miglitol: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic

glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Milnacipran: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and serotonin norepinephrine reuptake inhibitors (SNRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. There is also a case of a neuroleptic malignant syndrome-like reaction occurring in a child on chronic methylphenidate therapy after ingesting methylphenidate with an SNRI. It is unclear if the reaction was the result of a drug interaction. Monitor patients for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Minoxidil: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Mirtazapine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering drugs that have serotonergic properties such as methylphenidate derivatives and mirtazapine.
Modafinil: (Major) The use of modafinil with other psychostimulants, including methylphenidate or its derivatives, has not been extensively studied. Patients receiving combination therapy of modafinil with other psychostimulants should be closely observed for signs of nervousness, irritability, insomnia, arrhythmias, or other CNS stimulant-related side effects. Single dose studies of methylphenidate combined with modafinil noted that the rate of absorption of modafinil was delayed up to one hour by the presence of methylphenidate; no changes occurred in the metabolism and extent of absorption of either medication.
Moexipril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Monoamine oxidase inhibitors: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory

sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
Morphine: (Moderate) If concomitant use of morphine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Nadolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Nalbuphine: (Moderate) If concomitant use of nalbuphine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Nateglinide: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Nebivolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Nefazodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering drugs that have serotonergic properties such as methylphenidate derivatives and nefazodone. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
NiCARdipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate

derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
NIFEdipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
niMODipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Nisoldipine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Nitrates: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Nitroglycerin: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Nitroprusside: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Non-Ionic Contrast Media: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Methylphenidate derivatives should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Norepinephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Nortriptyline: (Moderate) Caution should be observed when coadministering

methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
OLANZapine; FLUoxetine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Oliceridine: (Moderate) If concomitant use of oliceridine and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Olmesartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Olmesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to

treat hypertension.
Opicapone: (Minor) Due to their pharmacologic actions, it is thought that increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and COMT inhibitors. Be alert for any dopamine-related side effects such as nausea, reduced appetite, tremor, or changes in moods or behaviors.
oxyCODONE: (Moderate) If concomitant use of oxycodone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
oxyMORphone: (Moderate) If concomitant use of oxymorphone and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
PARoxetine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Perindopril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Perindopril; amLODIPine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.

Perphenazine; Amitriptyline: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Phenelzine: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
PHENobarbital: (Moderate) Psychostimulants, such as methylphenidate derivatives, may lower the seizure threshold, thereby reducing the efficacy of anticonvulsants such as phenobarbital. Some human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of phenobarbital. More frequent monitoring of phenobarbital concentrations may be required when initiating or discontinuing methylphenidate. The mechanism of the potential effect on phenobarbital concentrations is not clear; methylphenidate is metabolized primarily to ritalinic acid by nonmicrosomal hydrolytic esterases that are widely distributed throughout the body, and appears to have no known inhibitory effect on hepatic enzymes.
PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Moderate) Psychostimulants, such as methylphenidate derivatives, may lower the seizure threshold, thereby reducing the efficacy of anticonvulsants such as phenobarbital. Some human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of phenobarbital. More frequent monitoring of phenobarbital concentrations may be required when initiating or discontinuing methylphenidate. The mechanism of the potential effect on phenobarbital concentrations is not clear; methylphenidate is metabolized primarily to ritalinic acid by nonmicrosomal hydrolytic esterases that are widely distributed throughout the body, and appears to have no known inhibitory effect on hepatic enzymes.
Phenoxybenzamine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate. Methylphenidates can reduce the hypotensive effect of antihypertensive agents such as alpha-blockers.
Phentolamine: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly

during initial coadministration and after dosage increases of methylphenidate. Methylphenidates can reduce the hypotensive effect of antihypertensive agents such as alpha-blockers.
Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Phenytoin: (Moderate) Monitor phenytoin concentrations during concomitant therapy with phenytoin and methylphenidate; a phenytoin dosage decrease may be necessary. Methylphenidate may inhibit the metabolism of phenytoin.
Pimozide: (Major) Pimozide should not be used in patients taking medicines that may, themselves, cause motor and phonic tics (e.g., methylphenidate) until such patients have been withdrawn from these drugs to determine whether or not the drugs, rather than Tourette's Disorder, are responsible for the tics. Once this issue is excluded, use together may proceed with caution.
Pindolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Pioglitazone: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Pioglitazone; Glimepiride: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones.

Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Pioglitazone; metFORMIN: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Potassium-sparing diuretics: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Pramipexole: (Moderate) Increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and dopamine agonists such as pergolide, pramipexole, apomorphine, and ropinirole. Dopaminergic side effects, such as nausea, loss of appetite, weight loss, insomnia, tremor, nervousness, or changes in mood or behavior, are possible.
Pramlintide: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Prazosin: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate. Methylphenidates can reduce the hypotensive effect of antihypertensive agents such as alpha-blockers.
Prilocaine; EPINEPHrine: (Moderate) Methylphenidate derivatives can potentiate the

actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Primidone: (Moderate) Psychostimulants, such as methylphenidate derivatives, may lower the seizure threshold, thereby reducing the efficacy of anticonvulsants such as primidone. Some human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of primidone, which is metabolized to phenobarbital. More frequent monitoring of drug concentrations may be required when initiating or discontinuing methylphenidate. The mechanism of the potential effect on primidone concentrations is not clear; methylphenidate is metabolized primarily to ritalinic acid by nonmicrosomal hydrolytic esterases that are widely distributed throughout the body, and appears to have no known inhibitory effect on hepatic enzymes.
Procarbazine: (Major) Because procarbazine exhibits some monoamine oxidase inhibitory (MAOI) activity, sympathomimetic drugs should be avoided. As with MAOIs, the use of a sympathomimetic drug with procarbazine may precipitate hypertensive crisis or other serious side effects. In the presence of MAOIs, drugs that cause release of norepinephrine induce severe cardiovascular and cerebrovascular responses. In general, do not use a sympathomimetic drug unless clinically necessary (e.g., medical emergencies, agents like dopamine) within the 14 days prior, during or 14 days after procarbazine therapy. If use is necessary within 2 weeks of the MAOI drug, in general the initial dose of the sympathomimetic agent must be greatly reduced. Patients should be counseled to avoid non-prescription (OTC) decongestants and other drug products, weight loss products, and energy supplements that contain sympathomimetic agents.
Promethazine; Phenylephrine: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Propranolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Protriptyline: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome

occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Quinapril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Quinapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Ramipril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Rasagiline: (Moderate) The concomitant use of rasagiline and sympathomimetics was not allowed in clinical studies; therefore, caution is advised during concurrent use of rasagiline and sympathomimetics including stimulants for ADHD and weight loss, non-prescription nasal, oral, and ophthalmic decongestants, and weight loss dietary supplements containing Ephedra. Although sympathomimetics are contraindicated for use with other non-selective monoamine oxidase inhibitors (MAOIs), hypertensive reactions generally are not expected to occur during concurrent use with rasagiline because of the selective monoamine oxidase-B (MAO-B) inhibition of rasagiline at manufacturer recommended doses. One case of elevated blood pressure has been reported in a patient during concurrent use of the recommended dose of rasagiline and ophthalmic tetrahydrozoline. One case of hypertensive crisis has been reported in a patient taking the recommended dose of another MAO-B inhibitor, selegiline, in combination with ephedrine. It should be noted that the MAO-B selectivity of rasagiline decreases in a dose-related manner as increases are made above the recommended daily dose and interactions with sympathomimetics may be more likely to occur at these higher doses.
Regular Insulin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin.

Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Regular Insulin; Isophane Insulin (NPH): (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Remifentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering remifentanil with methylphenidate derivatives. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Repaglinide: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Riociguat: (Major) Avoid use of sympathomimetic agents with riociguat. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including riociguat. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are

needed to avoid ischemia and other complications.
risperiDONE: (Moderate) Monitor for extrapyramidal symptoms (EPS) with concomitant use of risperidone and methylphenidate derivatives. Postmarketing cases of extrapyramidal symptoms (dystonia and dyskinesia) have been reported in patients when there was a change in dosage of either medication (increase or decrease in dosage) as well as with the initiation or discontinuation of either or both medications.
rOPINIRole: (Moderate) Increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and dopamine agonists such as pergolide, pramipexole, apomorphine, and ropinirole. Dopaminergic side effects, such as nausea, loss of appetite, weight loss, insomnia, tremor, nervousness, or changes in mood or behavior, are possible.
Rosiglitazone: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Sacubitril; Valsartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Safinamide: (Contraindicated) Safinamide, a selective monoamine oxidase-B inhibitor, is contraindicated for use with methylphenidate and its derivatives due to the risk of serotonin syndrome and hypertensive crisis. The manufacturer of safinamide recommends that a period of at least 14 days elapse between the discontinuation of safinamide and the initiation of serotonergic agents. Hypertensive crisis has been reported in patients taking recommended doses of selective MAO-B inhibitors and sympathomimetic medications, such as methylphenidate. Safinamide can cause hypertension or exacerbate existing hypertension, particularly at daily dosages exceeding those recommended by the manufacturer.
sAXagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking

medications for diabetes.
Selective serotonin reuptake inhibitors: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Selegiline: (Contraindicated) The product labels for methylphenidate and its derivatives contraindicate use with monoamine oxidase inhibitors (MAOIs), including selegiline, due to the risk of hypertensive crisis. Methylphenidate derivatives should not be used concurrently with selegiline or within 14 days before or after selegiline use.
Selexipag: (Major) Avoid use of sympathomimetic agents with selexipag. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including selexipag. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Semaglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Serdexmethylphenidate; Dexmethylphenidate: (Contraindicated) Avoid coadministration of methylphenidate and serdexmethylphenidate. These drugs represent duplicate treatments. Serious side effects such as nervousness, irritability, arrhythmias, palpitations, seizures, or other stimulant-related adverse effects may occur or get worse during concurrent use.
Serotonin norepinephrine reuptake inhibitors: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and serotonin norepinephrine

reuptake inhibitors (SNRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. There is also a case of a neuroleptic malignant syndrome-like reaction occurring in a child on chronic methylphenidate therapy after ingesting methylphenidate with an SNRI. It is unclear if the reaction was the result of a drug interaction. Monitor patients for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Sertraline: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Sevoflurane: (Major) Avoid the use of methylphenidate or its derivatives in patients being treated with halogenated anesthetics (e.g., enflurane, halothane, isoflurane, and methoxyflurane) on the day of surgery. The use of Metadate CD is contraindicated on the day of surgery. Halogenated anesthetics may sensitize the cardiovascular system to the effects of methylphenidate increasing the risk of sudden blood pressure and heart rate increase during surgery.
SGLT2 Inhibitors: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
SITagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking

medications for diabetes.
Sodium Oxybate: (Moderate) The stimulant effects of methylphenidate derivatives can be additive when used concurrently with other psychostimulants, such as sodium oxybate. The combination may increase the incidence of side effects; if these combinations cannot be avoided the patient should be closely observed for signs of nervousness, irritability, insomnia, arrhythmias, or other stimulant-related problems. Sodium oxybate has the potential to induce seizures; it has been speculated that this effect may be mediated through the action of sodium oxybate at GABA receptors. Although convulsant effects occur primarily at high dosages, sodium oxybate should be used cautiously with psychostimulants that are known to lower seizure threshold. Note that CNS stimulants, including methylphenidate, are frequently used in the treatment of narcolepsy, and clinical trials involving the use of psychostimulants with sodium oxybate have not found the combinations to be unsafe. Pharmacodynamic interactions cannot be ruled out, however.
Solriamfetol: (Moderate) Monitor blood pressure and heart rate during coadministration of solriamfetol, a norepinephrine and dopamine reuptake inhibitor, and methylphenidate derivatives, which are CNS stimulants. Concurrent use of solriamfetol and other medications that increase blood pressure and/or heart rate may increase the risk of such effects. Coadministration of solriamfetol with other drugs that increase blood pressure or heart rate has not been evaluated.
Sotagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Sotalol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Spironolactone: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Monitor blood

pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
St. John's Wort, Hypericum perforatum: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering methylphenidate derivatives and St. John's Wort. There are rare reports of serotonin syndrome occurring during use of other serotonergicagents and methylphenidate or its derivatives. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
SUFentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering sufentanil with methylphenidate derivatives. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Sulfonylureas: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Tapentadol: (Moderate) If concomitant use of tapentadol and methylphenidate derivatives is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Telmisartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Telmisartan; amLODIPine: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives.

Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Terazosin: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate. Methylphenidates can reduce the hypotensive effect of antihypertensive agents such as alpha-blockers.
Theophylline, Aminophylline: (Moderate) Concurrent administration of theophylline or aminophylline with sympathomimetics can produce excessive stimulation manifested by skeletal muscle activity, agitation, and hyperactivity.
Thiazide diuretics: (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Thiazolidinediones: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Thyroid hormones: (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Timolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Tirzepatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics.

Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Tolcapone: (Minor) Due to their pharmacologic actions, it is thought that increased dopaminergic effects may occur during coadministration of methylphenidate derivatives, inhibitors of dopamine reuptake, and COMT inhibitors. Be alert for any dopamine-related side effects such as nausea, reduced appetite, tremor, or changes in moods or behaviors.
Torsemide: (Moderate) Monitor blood pressure during concomitant loop diuretic and methylphenidate use; a loop diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
traMADol: (Moderate) Concurrent use of tramadol and methylphenidate derivatives might increase the risk for serotonin syndrome. If concomitant use is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome. There are also postmarketing reports of serotonin syndrome during concurrent use of methylphenidate or methylphenidate derivatives with other serotonergic medications.
Tramadol; Acetaminophen: (Moderate) Concurrent use of tramadol and methylphenidate derivatives might increase the risk for serotonin syndrome. If concomitant use is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome. There are also postmarketing reports of serotonin syndrome during concurrent use of methylphenidate or methylphenidate derivatives with other serotonergic medications.
Trandolapril: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors.
Trandolapril; Verapamil: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive

effect of antihypertensive agents such as angiotensin-converting enzyme inhibitors. (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Tranylcypromine: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
Treprostinil: (Major) Avoid use of sympathomimetic agents with treprostinil. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including treprostinil. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Triamterene: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Triamterene; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure during concomitant potassium-sparing diuretic and methylphenidate use; a potassium-sparing diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Tricyclic antidepressants: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical

management should be implemented.
Trimipramine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and tricyclic antidepressants (TCAs). There are postmarketing reports of serotonin syndrome occurring during use of methylphenidate derivatives and other serotonergic medications. Patients receiving this combination should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Umeclidinium; Vilanterol: (Moderate) Administer sympathomimetics with caution with beta-agonists such as vilanterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
Valsartan: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension.
Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and adjust the dose of the angiotensin II blockers as needed during coadministration with methylphenidate. Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. (Moderate) Monitor blood pressure during concomitant thiazide diuretic and methylphenidate use; a thiazide diuretic dose adjustment may be necessary. Methylphenidate may decrease the effectiveness of medications used to treat hypertension.
Vasodilators: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Vasopressin, ADH: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Vasopressors: (Moderate) Methylphenidate derivatives can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.

Venlafaxine: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and serotonin norepinephrine reuptake inhibitors (SNRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. There is also a case of a neuroleptic malignant syndrome-like reaction occurring in a child on chronic methylphenidate therapy after ingesting methylphenidate with an SNRI. It is unclear if the reaction was the result of a drug interaction. Monitor patients for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Verapamil: (Moderate) Periodic evaluation of blood pressure is advisable during concurrent use of methylphenidate derivatives and antihypertensive agents, particularly during initial coadministration and after dosage increases of methylphenidate derivatives. Methylphenidate derivatives can reduce the hypotensive effect of antihypertensive agents, including calcium-channel blockers.
Vilazodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering drugs that have serotonergic properties such as methylphenidate derivatives and vilazodone. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Patients receiving this combination should be monitored closely for toxicity. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Vortioxetine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering drugs that have serotonergic properties such as methylphenidate derivatives and vortioxetine. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Patients receiving methylphenidate derivatives with vortioxetine should be monitored for the emergence of serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical management should be implemented.
Warfarin: (Moderate) A dose adjustment of warfarin and more frequent INR monitoring may be required when initiating or discontinuing methylphenidate derivatives. Case reports suggest a potential interaction between methylphenidate derivatives and coumarin anticoagulants. Human pharmacologic studies have shown that methylphenidate derivatives may inhibit the metabolism of warfarin. The mechanism of the potential interaction is not clear. A dose adjustment of warfarin and more frequent monitoring of the INR may be required when initiating or discontinuing methylphenidate derivatives.

Adverse Reaction

insomnia

Centrally-mediated adverse reactions of methylphenidate are frequent but usually mild at normally prescribed dosages. These reactions may be more frequent or severe during initial therapy, and will likely diminish within a few weeks of continued use (i.e., tolerance occurs). Nervousness and insomnia (2% or more) are the most common adverse reactions to methylphenidate and may occur with all formulations. In both a 6-week open-label dose-optimization study of methylphenidate extended-release capsules (Jornay PM) in pediatric patients 6 to 12 years (n = 125, mean dose 50 mg) and a 3-week placebo-controlled study of Jornay PM in pediatric patients 6 to 12 years (n = 81; mean dose 52 mg), insomnia was the most frequently reported adverse effect, occurring in 33% to 41% of patients receiving Jornay PM. During a clinical trial of the methylphenidate transdermal system in adolescents 13 to 17 years of age with ADHD, insomnia occurred in 6.2% of those in the active transdermal treatment group (Daytrana). In children 6 to 12 years of age, insomnia occurred in 13.3% in the Daytrana group. Initial insomnia was associated with the use of methylphenidate extended-release oral suspension in 2% of children ages 6 to 12 years during clinical trials. Insomnia occurred in 13% of adults taking methylphenidate extended-release capsules (Adhensia XR) during clinical trials, with the highest incidence (19%) reported in adults taking 100 mg/day. During Adhansia XR clinical trials, 4% of adult patients reported feeling jittery. Insomnia occurred in 6% of pediatric patients (12 to 17 years) taking Adhansia XR, with the highest incidence (13%) in those receiving 85 mg/day. Insomnia was reported in 10% of pediatric patients 6 to 12 years during an open-label treatment phase. Insomnia occurred in 16.6% of adult patients receiving extended-release methylphenidate (Concerta). In pediatric patients 6 to 17 years of age receiving Concerta, insomnia occurred in 2.8% of methylphenidate-treated patients. In clinical trials of Concerta in adult and pediatric patients, insomnia was associated with discontinuation of the drug. Insomnia will typically resolve within a few days of use, provided the dosage is appropriate, and doses are not administered within 6 hours of bedtime. Avoidance of exercising late in the day, limiting caffeinated beverages, and setting regular bedtime schedules may limit sleep disruption. Continued interrupted sleep patterns may indicate a need for dosage reduction. Once-daily morning dosing of methylphenidate may be effective in some children and may also help to limit intolerable adverse reactions. If intolerable adverse reactions occur with the transdermal patch, either the dosage or wear time may be reduced. Individualization of wear time may help manage some adverse reactions caused by transdermal methylphenidate.

asthenia, dizziness, drowsiness, euphoria, fatigue, hyperactivity, lethargy, paresthesias, restlessness, seizures, tremor, vertigo

Centrally-mediated adverse reactions of methylphenidate are frequent but usually mild at normally prescribed dosages. These effects may be more frequent or severe during initial therapy, and will likely diminish within a few weeks of continued use. Nervousness is one of the most common adverse reactions of methylphenidate and may occur with all formulations; it has been reported in 2% or more of patients during placebo-controlled trials. Commonly reported (2% or more) adverse reactions in adults with ADHD from placebo-controlled trials of methylphenidate products include insomnia, nervousness, restlessness, dizziness, tremor, and vertigo. Mild euphoria and restlessness may be noted in the first weeks of treatment. Restlessness was reported in 3.1% of adults receiving extended-release methylphenidate (Concerta) during clinical trials. Other CNS reactions occurring more often in adult and pediatric patients receiving Concerta than those receiving placebo included vertigo (1.7%) and dizziness (1.9% to 6.7%) and paresthesias (1.2%). During a clinical trial of the methylphenidate transdermal system (Daytrana) in adolescents 13 to 17 years of age with ADHD, dizziness occurred in 5.5% of patients receiving Daytrana and more often than in patients receiving placebo; paresthesias were also reported. Motion sickness was reported in 2% of patients taking the extended-release suspension. Dizziness was reported in 3% of pediatric patients (12 to 17 years) receiving methylphenidate extended-release capsules (Adhansia XR) during clinical trials. Psychomotor hyperactivity occurred in 5% of children 6 to 12 years receiving methylphenidate extended-release capsules (Jornay PM) during open-label or placebo-controlled evaluations. Drowsiness, lethargy, and fatigue have also been reported with most methylphenidate dosage forms. Once-daily morning dosing of methylphenidate may be effective in some patients and may also help to limit intolerable adverse reactions. If intolerable adverse reactions occur with the transdermal patch, either the dosage or wear time may be reduced. Individualization of wear time may help manage some of the adverse reactions caused by transdermal methylphenidate. Asthenia, seizures, and reversible ischemic neurological deficit have been reported during postmarketing use of some formulations of methylphenidate, although the frequency is unknown and causality to the drug has not been established.

headache, migraine

Headache is a commonly occurring neurological effect of methylphenidate; however, the headaches are generally mild and may respond to a dosage reduction. During separate clinical trials of the methylphenidate transdermal system (Daytrana), extended-release chewable tablets (QuilliChew ER), and biphasic-release methylphenidate (Metadate CD and Aptensio XR) in adults, adolescents, and children 6 to 12 years of age, headache

occurred in 2.4% to 15.3% of patients who received methylphenidate compared to 0% to 12.5% of those who received placebo. In addition, headache was one of the most common adverse reactions associated with the discontinuation of Daytrana in children. Headache occurred in 10% to 19% of children 6 to 12 years receiving methylphenidate extended-release capsules (Jornay PM) during open-label or placebo-controlled evaluations. Headache was reported in 10% of children ages 6 to 12 years during methylphenidate extended-release capsules (Adhansia XR) treatment. Headache and tension headache occurred in 22.2% and 1.2% of adult patients receiving extended-release methylphenidate (Concerta) compared to 15.6% and 0.5% of those receiving placebo, respectively. Migraine headaches have also been reported during postmarketing use of various methylphenidate products; however, the frequency is unknown, and causality to the drug has not been established.

abdominal pain, anorexia, constipation, diarrhea, dyspepsia, nausea, teeth grinding (bruxism), vomiting, weight loss, xerostomia

Gastrointestinal (GI) reactions, particularly abdominal discomfort and decreased appetite, are commonly associated with methylphenidate use. Commonly reported (2% or more of the methylphenidate group and at least twice the rate of the placebo group) GI adverse reactions from placebo-controlled trials of methylphenidate products include: appetite decreased, weight decreased, nausea, abdominal pain, dyspepsia, xerostomia, and vomiting. Anorexia (reported as loss or decrease of appetite) and other appetite changes occur in many patients in the first days of therapy. Anorexia and weight loss appear to occur more frequently in children compared to adults, particularly during prolonged therapy. An FDA analysis reported children younger than 6 years receiving extended-release stimulants have higher medication exposure and significant weight loss (at least 10% decrease) compared to older children on the same dose. Due to these findings, the benefits may not outweigh the risks in this age group. In a study of 4 and 5 year olds receiving extended-release methylphenidate (Aptensio XR), high rates of adverse reactions, most notably weight loss, were experienced. When weights were compared to those prior to initiation, 20 of 39 patients had lost enough weight to decrease 10 or more percentiles on the CDC growth chart for weight. During a clinical trial of the methylphenidate transdermal system (Daytrana) in adolescents 13 to 17 years of age with ADHD, the most common GI reactions included decreased appetite (25.5%), weight loss (5.5%), and nausea (9.7%). Less frequently reported GI reactions that occurred more often in the active group than the placebo group included abdominal pain (4.8%), vomiting (3.4%), and anorexia (4.8%). Decreased appetite and anorexia were among the most frequently reported adverse reactions leading to discontinuation in the Daytrana group (1.4%). In children 6 to 12 years of age, GI reactions that occurred more often in the Daytrana group than in the placebo group included decreased appetite (25.5%), nausea (12.2%), vomiting (10.2%), weight loss (9.2%), abdominal pain (7.1%), and

anorexia (5.1%). GI reactions that occurred more often in children and adolescents receiving extended-release methylphenidate (Concerta) than placebo included upper abdominal pain (6.2%) and vomiting (2.8%); decreased appetite and weight loss were reported in 25.3% and 6.5% of adults, respectively. Other GI reactions that occurred more often in adults receiving Concerta than placebo included xerostomia (14%), nausea (12.8%), dyspepsia (2.2%), vomiting (1.7%), constipation (1.4%), and anorexia (1.7%). Diarrhea was also reported in patients receiving Concerta in clinical trials. Anorexia and abdominal pain were also common reactions in pediatric patients with ADHD receiving biphasic-release methylphenidate (Metadate CD), occurring in 9% and 7% of patients, respectively. During a clinical trial of methylphenidate extended-release capsules (Adhensia XR) in adult patients, GI adverse reactions were reported more frequently in patients receiving the 70 mg and/or 100 mg doses compared to all doses. The following GI adverse reactions were reported in adult patients: xerostomia (14% for 100 mg vs. 8%), nausea (11% for 100 mg vs. 5%), diarrhea (7% for 70 mg and 5% for 100 mg vs. 3%), anorexia (15% for 70 mg and 19% for 100 mg vs. 9%), and weight loss (5% for 100 mg vs. 3%). In pediatric patients (12 to 17 years), upper abdominal pain was reported in 4% of patients. For the following GI adverse reactions, the reported incidence was greater in pediatric patients who received the 70 mg and/or 85 mg doses compared to all doses: anorexia (28% for 70 mg and 26% for 85 mg vs. 20%), nausea (7% for 70 mg and 8% for 85 mg vs. 6%), xerostomia (5% for 70 mg and 4% for 85 mg vs. 3%), vomiting (6% for 85 mg vs. 3%), and weight loss (8% for 70 mg and 13% for 85 mg vs. 7%). Pediatric patients (6 to 12 years) reported anorexia (35%), upper abdominal pain (15%), nausea or vomiting (13%), and weight loss (12%) during an open-label clinical trial. Anorexia (2% to 27%), upper abdominal pain (8% to 9%), nausea (3.8% to 9%), and vomiting (2% to 9%) have all been prevalent in pediatric clinical trials of multiple once-daily methylphenidate formulations. Teeth grinding (bruxism) has been reported postmarketing. Eating small, frequent meals or snacks may help limit appetite problems. Continued decreased appetite or weight loss may indicate a need for dosage reduction. Complaints of xerostomia may be limited by sucking sugarless hard candy, crushed ice, and drinking plenty of water or other fluids. Most adverse reactions disappear within a few weeks of continued use (i.e., tolerance occurs). Once-daily morning dosing of methylphenidate may be effective in some children and may also help to limit intolerable adverse reactions. If intolerable adverse reactions occur with the use of the methylphenidate transdermal patch, either the dosage or wear time may be reduced. Individualization of wear time may help manage some of the adverse reactions caused by transdermal methylphenidate.

growth inhibition

Data are inadequate to determine whether chronic use of stimulants, such as methylphenidate, causes long-term growth inhibition. Although data are limited,

available studies do not indicate that stimulant use compromises the attainment of normal adult height and weight in most children. Practitioners should monitor height and weight parameters relative to age at treatment initiation and periodically thereafter (at minimum yearly). Patients who are not growing or gaining weight as expected may need to have their treatment interrupted. In a 24-month follow-up, the MultiModal Treatment Study showed a deceleration of growth of roughly 1 cm per year with stimulant use. In general, growth remained in the normal curve for most children, except those in the lowest percentiles of height for age. Data obtained on the effects of stimulants on growth suppression in children 7 to 10 years of age suggested that regularly medicated children (7 days/week throughout the year) had a temporary average slowing in growth of 2 cm in height and 2.7 kg in weight over 3 years. Reduction of annual growth rate was maximal in the first year, decreased in the second year, and absent in the third year of treatment; however, no compensatory growth rebound effects were found while on stimulant therapy. In clinical trials of methylphenidate, some degree of weight loss occurred in approximately 5% to 10% of pediatric patients. Proposed mechanisms of growth inhibition include the suppression of appetite or an alteration in growth hormone secretion. Some experts recommend the use of drug holidays to allow growth to 'catch-up'. However, drug holidays are typically reserved for children with well-controlled attention-deficit hyperactivity disorder (ADHD) symptoms and are of unproved value in limiting growth suppression.

agitation, anxiety, confusion, depression, emotional lability, hallucinations, hostility, irritability, libido decrease, mania, psychosis, suicidal ideation, supranormalization

Various psychiatric effects have been reported during treatment with stimulants such as methylphenidate. Commonly reported adverse reactions in adults with ADHD from placebo-controlled trials of methylphenidate include anxiety (2% to 8.2%), depressed mood (3.9%), agitation (2% to 2.2%), aggression (1.7%), depression (1.7%), libido decrease (1.7%), confusion (1.2%), sedation (1.2%), and tension (1.2%). Other psychiatric effects reported in methylphenidate clinical trials included anger, hypervigilance, mood alterations, tearfulness, and panic attacks. Nervousness is one of the most common adverse effects of methylphenidate and may improve with a dosage reduction or omitting the afternoon dose for products that are dosed multiple times per day. Methylphenidate may aggravate pre-existing symptoms such as anxiety, tension, and agitation. Stimulants can cause new-onset psychotic or manic symptoms (i.e., hallucinations, psychosis, delusional thinking, or mania). These symptoms occurred in approximately 0.1% of patients treated with stimulants (methylphenidate or amphetamine at usual doses) in a pooled analysis of short-term, placebo-controlled studies. In a cohort study assessing 221,846 adolescents and young adults who received a prescription for a stimulant for ADHD, new-onset psychosis occurred in approximately

1 in 660 patients. The percentage of patients who had a psychotic episode was 0.1% in patients receiving methylphenidate compared to 0.21% in patients receiving amphetamine (HR with amphetamine use, 1.65; 95% CI 1.31 to 2.09). The median time from when the stimulant was dispensed to the psychotic episode was 128 days. Advise patients and their caregivers to promptly report any changes in mood or behavior. If suicide-related events emerge during treatment, consider dose reduction or drug discontinuation, especially if symptoms are severe, abrupt in onset, or were not part of the presenting symptoms of the patient. Nervousness, irritability (6% to 11%), and emotional lability (2.4% to 22%) were the most common psychiatric reactions reported during pediatric trials of methylphenidate; anxiety and depressed mood occurred less frequently. Irritability was associated with discontinuation of Daytrana in adolescents. Once-daily morning dosing of methylphenidate may be effective in some children and may help to limit intolerable side effects. If intolerable adverse reactions occur with the transdermal patch, either the dosage or the wear time may be reduced. Patients with ADHD who become overly preoccupied with a task (overfocused or inflexible) or are described as 'zombie-like' are considered to exhibit supranormalization; these behaviors typically require dosage reduction. During postmarketing use of methylphenidate products, disorientation, auditory and visual hallucinations, logorrhea, mania, abnormal behavior, aggression, anxiety, nervousness, hostility, depression, obsessive-compulsive disorder, and suicidal ideation and behaviors (including completed suicide) have been reported. In addition, severe depression may occur during abrupt discontinuation after abusive use of methylphenidate; monitor patients carefully. While centrally-mediated effects are relatively common with both ADHD and typical methylphenidate use, excessive symptoms (agitation, confusion, and hallucinations) might represent excessive dosage and toxicity. Methylphenidate has been reported as a frequently suspected drug in serious adverse reactions in children, according to the Institute for Safe Medication Practices (ISMP). Of the serious adverse reactions reported to the FDA during a 5-year time span (2008 to 2012), sudden death and psychiatric effects (aggression, suicidal behaviors, psychotic episodes) were predominant for methylphenidate. Because reports submitted to the FDA likely represent only a portion of actual events and may be skewed, further investigation to determine frequency of occurrence and causality to the drug is warranted.

dyskinesia, tics, Tourette syndrome

Dyskinesia has been reported during postmarketing use of CNS stimulants, including methylphenidate. The onset or exacerbation of motor and verbal tics has also been reported. Individuals should be monitored for the emergence or worsening of dyskinesias, tics or Tourette syndrome; consider dose reduction or discontinuation of treatment if clinically indicated.

angina, arrhythmia exacerbation, bradycardia, chest pain (unspecified), hypertension, myocardial infarction, palpitations, sinus tachycardia, stroke, supraventricular tachycardia (SVT), syncope, vasculitis

Methylphenidate-induced increases in blood pressure and heart rate have been reported in 2% or more of patients during clinical trials for various methylphenidate products. CNS stimulants cause an increase in blood pressure (mean increase approximately 2 to 4 mmHg) and heart rate (mean increase approximately 3 to 6 bpm). Selected individuals may have larger increases. Hypertension may occur in rare individuals. Monitor blood pressure and heart rate at baseline, after dosage increases, and periodically throughout methylphenidate therapy. Sinus tachycardia has been reported in 0.7% and 1% of adolescents and children, respectively, receiving transdermal therapy (Daytrana) and 2% to 8% of pediatric patients and 2% to 5% of adult patients with various oral products. Palpitations were experienced by 3.1% of adults in some clinical trials. Cardiovascular events, including sudden death, have been associated with stimulant use in pediatric patients with structural cardiac abnormalities or other serious heart problems. Cardiovascular and cerebrovascular effects associated with methylphenidate use range in severity from mild to life-threatening and include cardiac murmur, palpitations, angina, chest pain (unspecified), cardiac arrhythmia (arrhythmia exacerbation) including supraventricular tachycardia (SVT), sinus tachycardia, bradycardia, extrasystole, myocardial infarction (reported in adults), stroke (reported in adults), and cerebral arteritis (vasculitis) or occlusion. The presence of any serious heart rate increases, blood pressure increase, or cardiovascular event requires evaluation and consideration of drug discontinuation. Pediatric patients who develop symptoms such as exertional chest pain (unspecified), unexplained syncope, or other symptoms suggestive of cardiac disease during methylphenidate treatment should undergo a prompt cardiac evaluation. Such cardiac adverse reactions may be associated with methylphenidate toxicity; evaluate patients carefully who present with cardiac symptoms for possible overdose. During a 5-year time span (2008 to 2012), 37 cases of sudden death associated with methylphenidate use in pediatric patients were reported to the FDA; however, causality to the drug has not been established. In a nationwide self-controlled case series (n = 1,224), use of methylphenidate in children and adolescents was associated with an increased risk of arrhythmia during the first 8 weeks of therapy (incidence rate ratio [IRR] 1.61; 95% CI 1.48 to 1.74), with the highest risk observed within the first 3 days of treatment (IRR 2.01; 95% CI 1.74 to 2.31) and in those with congenital heart disease (IRR 3.49; 95% CI 2.33 to 5.22). Overall, no significant risk of myocardial infarction was observed, but risk was elevated after the first week of treatment through week 8.

hyperhidrosis

Hyperhidrosis (increased sweating) has been reported in at least 2% of pediatric and adult patients receiving methylphenidate products in controlled clinical trials, and at rates at least twice the rate of the placebo group. Some products reported increased sweating in up to 5.1% of adults during clinical trials. Excessive sweating has been associated with methylphenidate toxicity; evaluate a patient who presents with complaints of increased sweating for other symptoms of possible toxicity or need for dose adjustment. Thirst has been reported during extended-release methylphenidate (Concerta) postmarketing use.

alopecia, anaphylactoid reactions, angioedema, bullous rash, erythema, erythema multiforme, exfoliative dermatitis, pruritus, purpura, rash, urticaria

Hypersensitivity reactions to oral methylphenidate are infrequent and have included skin rash (unspecified) (2%), urticaria, hyperpyrexia, arthralgia, exfoliative dermatitis, and erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura. Angioedema, anaphylactoid reactions, alopecia, urticaria, rash, rash (erythematous), macular rash, auricular swelling, bullous rash conditions, exfoliative dermatitis, eruptions, erythema, and exanthemas have been reported during postmarketing use of methylphenidate products. Some skin reactions may be accompanied by pruritus. Excoriation occurred in 4% of pediatric patients during clinical trials of methylphenidate extended-release oral solution. Contusion was reported in 3% of patients receiving Jornay PM and more frequently than in patients receiving placebo during clinical trials.

atopic dermatitis, chemical leukoderma, contact dermatitis, ecchymosis, skin erosion, skin hyperpigmentation, skin hypopigmentation, skin irritation, xerosis

Chemical leukoderma, a condition that causes the skin to lose color from repeated exposure to specific chemical compounds, may occur with use of the methylphenidate patch. The condition is not physically harmful, but it is disfiguring and is thought to be irreversible, which may cause emotional distress. The areas of skin color loss described with the methylphenidate patch have ranged up to 8 inches in diameter, with a time of onset ranging from 2 months to 4 years after starting the patch. Skin hypopigmentation has occurred under and around the patch, and less frequently on parts of the body where the patch was never applied. Chemical leukoderma can mimic the appearance of vitiligo, particularly at remote sites of skin hypopigmentation. Individuals with a history of vitiligo and/or a family history of vitiligo may be more at risk. Patients and caregivers should be advised to watch for new areas of lighter skin, especially under the drug

patch, and immediately report these changes to their health care providers. Alternative treatment should be considered in patients who experience these skin changes. Erythema and pruritus occur commonly during use of transdermal methylphenidate. Use of transdermal methylphenidate may lead to a contact sensitization or skin irritation such as allergic contact dermatitis. Application site reactions resulted in patient withdrawal in roughly 6.7% of children and 1.9% of adolescents in methylphenidate patch long-term (up to 6 to 12 months) trials. In an open-label study designed to assess dermal reactions to the Daytrana patch in children with ADHD (n = 305), 1 patient (0.3%) experienced allergic contact dermatitis consisting of erythema and edema at the patch application site with concurrent urticarial lesions on the abdomen and legs. During postmarketing use of transdermal methylphenidate, application site reactions have included bleeding, bruising (ecchymosis), burning, discharge, discoloration, discomfort, dryness (xerosis), eczema (atopic dermatitis), edema, skin erosion, excoriation, exfoliation, fissure, skin hyperpigmentation, skin hypopigmentation, induration, infected skin, inflammation, skin irritation, pain, papules, paresthesias, rash, scab, swelling, ulcer, urticaria, vesicles, and warmth. Patients should alternate hip application sites each day to help prevent sensitization. If skin irritation develops, the patch should be removed. Erythema at the site of application is not always indicative of an allergic reaction; however, if contact sensitization is suspected (i.e., there is also edema, papules, or vesicles that do not significantly improve within 24 hours to 48 hours or spread beyond the patch site) the methylphenidate patch should be discontinued. Patients who develop contact dermatitis with transdermal methylphenidate may also be sensitized to oral methylphenidate and should be initiated on oral therapy under close supervision. Some patients who develop sensitization to the patch may not be able to use the oral products. Patients sensitized from use of transdermal methylphenidate, as evidenced by development of an allergic contact dermatitis, may develop systemic sensitization with subsequent use of oral methylphenidate. Manifestations of systemic sensitization may include a flare-up of previous dermatitis or of prior positive patch test sites, or generalized skin eruptions in previously unaffected skin. Other systemic reactions may include headache, hyperpyrexia, malaise, arthralgia, diarrhea, or vomiting.

peripheral vasoconstriction, skin ulcer

Stimulants used to treat ADHD, including methylphenidate, are associated with peripheral vasculopathy. Effects of peripheral vasoconstriction, including Raynaud's phenomenon, were observed in postmarketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms are usually intermittent and mild and generally improve after reduction in dose or discontinuation of drug. However, very rare sequelae include digital skin ulcer and/or soft tissue breakdown. Carefully monitor for digital changes during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be

appropriate for certain patients. Additionally, during postmarketing use of extended-release methylphenidate, peripheral coldness has been reported, although the frequency is unknown and causality to the drug has not been established.

arthralgia, back pain, muscle cramps, myalgia

During a 3-week placebo-controlled trial in pediatric patients 6 to 12 years (n = 81; mean dose 52 mg), back pain was reported in 3% of patients receiving Jornay PM and more frequently than in patients receiving placebo. Muscle tightness (1.9%) has been reported in adults receiving extended-release methylphenidate (Concerta) during clinical trials. Arthralgia, myalgia, muscle cramps, and muscle twitching have been reported during postmarketing use of methylphenidate products; however, the incidences are unknown, and causality to the drug has not been established.

anemia, leukopenia, pancytopenia, thrombocytopenia

Hematologic abnormalities including anemia, thrombocytopenia, leukopenia, and other blood dyscrasias have occurred rarely during treatment with methylphenidate; however, causality has not been established. Abnormal white blood cell count, leukopenia, pancytopenia, thrombocytopenia, and thrombocytopenic purpura have been reported during postmarketing use. Periodic blood counts and platelet counts may be advisable for those on chronic treatment with methylphenidate as a precaution.

elevated hepatic enzymes, hepatic failure, hyperbilirubinemia

In rare instances, elevated hepatic enzymes (e.g., elevated alanine aminotransferase), acute hepatic failure, and hepatocellular injury have occurred during treatment with methylphenidate; however, causality has not been established. Elevated alkaline phosphatase and hyperbilirubinemia have also been reported.

blurred vision, diplopia, mydriasis, ocular hypertension, ocular pain, visual impairment

Ocular pain has been reported in 2% of pediatric patients during clinical trials of methylphenidate. Ocular reactions such as visual impairment, blurred vision, mydriasis, diplopia, dry eye, and accommodation disorder have been reported during postmarketing experience with various methylphenidate products. Blurred vision occurred in 1.7% of adult patients who received extended-release methylphenidate during clinical trials compared to 0.5% of patients who received placebo, and in 2% or more of patients during clinical trial experience with other methylphenidate products in children, adolescents, and adults. The sympathetic stimulation from stimulants may block aqueous outflow and may raise intraocular pressure, exacerbating ocular

hypertension or glaucoma. Patients are encouraged to report any unusual changes in vision promptly for examination and evaluation.

cough, dyspnea, infection, pharyngitis, sinusitis

Respiratory adverse reactions occurring in adults receiving methylphenidate include upper respiratory tract infection (2% to 2.2%) and oropharyngeal pain (1.7%). Respiratory adverse reactions occurring in children and adolescents receiving methylphenidate include naso-pharyngitis (2.8% to 3%), streptococcal pharyngitis (3%), cough (1.9%), upper respiratory tract infection (17%), and oropharyngeal pain (1.2%). Sinusitis and dyspnea have been reported during postmarketing use of methylphenidate; however, the frequencies are unknown.

gynecomastia, priapism

Frequent or prolonged erections and priapism have been reported during use of stimulant and non-stimulant medications for ADHD. Reported cases of priapism have occurred after a period of time on stimulant therapy and often subsequent to a dose increase. Priapism has also been reported during periods of drug withdrawal (e.g., drug holidays or discontinuation). Prolonged erections in male patients should be promptly reported, as immediate diagnosis and treatment are essential to avoid tissue damage. Priapism can occur in males of any age; younger males, particularly those who have not reached puberty, may not recognize the problem or may be embarrassed to tell anyone if it occurs. In a review of methylphenidate products by the FDA, the median age of patients who experienced priapism was 12.5 years (range: 8 to 33 years). Caution should be used when considering changing male patients from stimulant to non-stimulant medications; atomoxetine is also associated with priapism in young males and appears to carry a higher risk of the condition compared to methylphenidate. Gynecomastia has also been reported during postmarketing experience with some formulations of methylphenidate products.

neuroleptic malignant syndrome

Very rare cases of a neuroleptic malignant syndrome (NMS) have been reported. In most of these cases, patients were concurrently receiving therapies associated with NMS along with methylphenidate. In a single report, a 10-year-old boy who had been taking methylphenidate for approximately 18 months experienced an NMS-like event within 45 minutes of ingesting his first dose of venlafaxine. It is uncertain whether this case represented a drug-drug interaction, a response to either drug alone, or some other cause.

fever, hot flashes

Fever (pyrexia) has been associated with methylphenidate use. Pyrexia was reported in 2% or more of adults with ADHD receiving methylphenidate products during clinical trials. Fever occurred in 2.2% of children and adolescents who received extended-release methylphenidate during clinical trials. During postmarketing use, hyperpyrexia and hot flashes have been reported, although the frequencies of these are unknown. Fever, sometimes severe enough to require external cooling, is also associated with methylphenidate toxicity or may be a symptom of neuroleptic malignant syndrome (NMS); carefully evaluate the patient for other signs and symptoms of overdose or NMS if fever occurs.

serotonin syndrome

Serotonin syndrome in combination with other serotonergic drugs has been reported during postmarketing use of methylphenidate, although the frequency is unknown and causality has not been established. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. If serotonin syndrome becomes evident during methylphenidate treatment, methylphenidate and any other serotonergic agents should be discontinued and appropriate medical treatment should be initiated.

coma, delirium, diaphoresis, hyperthermia, paranoia, rhabdomyolysis

Rhabdomyolysis has been associated with the use of stimulants used to treat attention-deficit hyperactivity disorder; stimulant-induced rhabdomyolysis is most often associated with sympathomimetic toxicity and has been reported in postmarketing use of methylphenidate products. Toxic effects of methylphenidate are more variable in children than in adults and appear to occur over a wide dosage range. Practitioners should be alert to the signs of excessive dosages or overdose which may include any of the following signs of CNS overstimulation or sympathomimetic effects: angina, anxiety, agitation, biting, blurred vision, delirium, diaphoresis, flushing or pallor, hallucinations, hyperthermia, labile blood pressure and heart rate (hypotension or hypertension), mydriasis, palpitations, paranoia, purposeless movements, psychosis, sinus tachycardia, tachypnea, or tremor. Severe manifestations of methylphenidate overdose include cardiac arrhythmias including heart block, circulatory collapse, rhabdomyolysis, seizures, coma, and death. If overdose is suspected with the use of the methylphenidate patch, the patch should be removed immediately and the area cleaned. The continued absorption of methylphenidate from the skin may occur after the patch is removed. Treatment consists of appropriate supportive measures, emergency transport and/or immediate contact with a Poison Control Center.

physiological dependence, psychological dependence, tolerance, withdrawal

Psychological dependence, physiological dependence, and tolerance may occur with methylphenidate therapy. Abrupt discontinuation or a significant dose reduction of CNS stimulants after prolonged use may produce withdrawal symptoms that include dysphoria, depression, fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite, and psychomotor retardation or agitation.

hematuria

Hematuria has been reported in postmarketing use of methylphenidate-containing products.

Description

Methylphenidate is a central nervous system stimulant that is chemically similar to the amphetamines. The peripheral pharmacologic actions of methylphenidate are milder than those of the amphetamines; it has more noticeable effects on central functioning than on motor activities. Methylphenidate is indicated for use in attention-deficit hyperactivity disorder (ADHD) and narcolepsy. It is occasionally used off-label for post-stroke depression or other depressive disorders refractory to other treatments. Stimulants are considered first-line agents in the treatment of ADHD. Methylphenidate and other stimulants are highly effective for the treatment of ADHD, with few comparative differences in efficacy. Two well-controlled trials demonstrate that roughly 70% to 80% of children treated with stimulants will have improvements such that at the end of the treatment phase the child no longer meets criteria for diagnosis of ADHD. Methylphenidate has been shown to have a strong effect on measures of attention, distractibility, impulsivity, and social and classroom behavior. Modest effect sizes have been reported for academic achievement. Lack of response to 1 stimulant does not predict a response to other stimulants, and a trial with a different agent (i.e., dexmethylphenidate, dextroamphetamine, mixed amphetamine salts) may be warranted if treatment fails with the initial stimulant. The Preschool ADHD Treatment Study (PATS), funded by the National Institute of Mental Health, provides important clinical guidance for children 3 to 5 years of age with ADHD. Stimulants have been associated with sudden death in patients with structural cardiac abnormalities or other serious cardiac disease when used at recommended ADHD doses; patients with structural heart defects, cardiomyopathy, coronary artery disease, serious cardiac arrhythmias, or other serious cardiac disease may be at risk for adverse cardiac events. The American Academy of Pediatrics and the American Heart Association recommend

careful screening of all children and adolescents prior to initiating pharmacologic therapy for ADHD, including a detailed patient and family history and physical examination; any significant findings should be further assessed and referred for consultation with a pediatric cardiologist prior to initiating treatment.

Mechanism Of Action

Methylphenidate is a central nervous system (CNS) stimulant that is chemically similar to the amphetamines. Methylphenidate is a racemic mixture comprised of the d- and l-threo enantiomers. The d-threo enantiomer is more pharmacologically active than the l-threo enantiomer. The exact mechanism of action of methylphenidate for the treatment of attention-deficit hyperactivity disorder (ADHD) and narcolepsy is not established. Methylphenidate is an indirect agonist; it inhibits the reuptake of dopamine and norepinephrine, facilitating their release into the synaptic cleft. As a result, sympathomimetic activity in the CNS is increased. There is some evidence that the alteration of dopamine transport systems by methylphenidate may indirectly augment the action of serotonin, but further pharmacologic research is needed to understand these processes. The main sites of CNS activity appear to be the brain stem arousal system and the cerebral cortex, including the subcortical structures of the thalamus. Methylphenidate-induced CNS stimulation produces a decreased sense of fatigue, an increase in motor activity and mental alertness, and mild euphoria. Improved attention spans, decreased distractibility, increased the ability to follow directions or complete tasks, and decreased impulsivity and aggression are noted when stimulants are prescribed for the treatment of ADHD. Unlike the amphetamines and cocaine, physical dependence is infrequent with clinical use at therapeutic doses. Chronic use of methylphenidate may lead to tolerance of side effects and psychological dependence, similar to other psychostimulants. Psychological dependence and addiction are more likely with parenteral or inhalational abuse or other illicit use. In the periphery, the sympathomimetic actions of methylphenidate are minimal at therapeutic doses. Heart rate typically increases slightly with normal therapeutic doses of stimulants (about 3 to 6 bpm); however, a reflexive decrease in heart rate in response to increased blood pressure can also occur. At high doses, such as in overdoses, stimulants can cause significant hypertension, tachycardia, arrhythmias, and other serious complications.

Pharmacokinetics

Methylphenidate is administered orally and transdermally. It is a racemic mixture comprised of the d- and l-threo enantiomers, the d-enantiomer being more pharmacologically active. The distribution of methylphenidate in humans is unknown, but the agent does cross the blood-brain-barrier with high regional uptake in the

striatum. The low degree of protein binding and high lipid solubility indicate that methylphenidate largely penetrates the central nervous system (CNS). Plasma protein binding is 10% to 33%. Therapeutic activity is primarily due to the parent compound. Metabolism of methylphenidate occurs in the liver via de-esterification to the primary metabolite alpha-phenyl-piperidine acetic acid (PPA, ritalinic acid), which has little pharmacologic activity. Small amounts of the hydroxylated metabolites (e.g., hydroxymethylphenidate and hydroxyritalinic acid) are detectable in plasma. In studies with methylphenidate tablets and extended-release capsules (Ritalin LA), the average elimination half-life in adults is approximately 3.5 hours (range: 1.3 to 7.7 hours) and in children is approximately 2.5 hours (range 1.5 to 5 hours). The half-life of methylphenidate after oral administration of Jornay PM is about 5.9 hours. Most of a methylphenidate dose is recovered in urine (90%), primarily as ritalinic acid, which accounts for about 80% of the dose.

Affected cytochrome P450 isoenzymes and drug transporters: none
Methylphenidate is not metabolized by the cytochrome P450 system to a clinically significant extent and does not appear to be a relevant inhibitor of CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A.

Route-Specific Pharmacokinetics

- **Oral Route**

The rapid half-life of immediate-release oral preparations may result in unmeasurable concentrations of the drug between the morning and midday doses; extended-release preparations reduce these peak and trough variances. Extended-release once-daily oral preparations minimize the fluctuations between peak and trough concentrations associated with immediate-release formulations. The transdermal form of methylphenidate bypasses the liver upon first pass, unlike the oral formulation, resulting in higher serum concentrations with lower initial doses. Additionally, the concentration of l-methylphenidate is roughly equal to that of d-methylphenidate with patch administration, whereas with oral administration little l-methylphenidate is available due to first pass metabolism. However, the pharmacological activity of l-methylphenidate is less than d-methylphenidate.
Immediate-release and extended-release dosage forms dosed more than once per day: Peak serum concentrations are achieved in about 1.9 hours and 4.7 hours for the regular and extended-release forms, respectively. The duration of action ranges from 3 to 6 hours with regular tablets and about 8 hours with the extended-release tablets.
Concerta: These extended-release tablets for once daily administration follow a biphasic pharmacokinetic profile to provide day-long medication availability. After oral administration of Concerta, plasma concentrations of methylphenidate increase rapidly reaching an initial maximum at about 1 hour, followed by a gradual increase in

concentration over the next 5 to 9 hours. Thereafter, concentrations gradually decrease. Tmax across all doses occurs between 6 to 10 hours. The half-life of methylphenidate in adolescents after oral administration of Concerta is about 3.5 hours.
Metadate CD: These extended-release capsules for once-daily administration follow a biphasic pharmacokinetic profile to provide day-long medication availability. Using Diffucaps technology, the capsules contain the drug in both rapid release and continuous release beads such that 30% of the dose is rapidly released and 70% of the dose is continuously released. The product demonstrates an initial peak plasma concentration at about 1.5 hours and a second peak at about 4.5 hours. The Metadate CD capsule, when opened and sprinkled on a tablespoon of cool applesauce, is bioequivalent to the intact capsule. The mean terminal half-life of Metadate CD in adults is 6.8 hours (compared to 2.9 hours for immediate release and 3.4 hours for sustained release).
Ritalin LA: These extended-release capsules for once-daily administration follow a biphasic pharmacokinetic profile to provide day-long medication availability. Using SODAS technology, the capsules contain the drug in both rapid release and continuous release beads such that 50% of the dose is rapidly released and 50% of the dose is continuously released from enteric coated, delayed-release beads. The effects of altered gastric pH on the absorption of Ritalin LA have not been studied. Interactions with antacids or acid blockers are possible. The absolute oral bioavailability in children is 22 +/- 8% for d-methylphenidate and 5 +/- 3% for l-methylphenidate, which is suggestive of significant pre-systemic metabolism. The product demonstrates an initial peak plasma level at about 1 to 3 hours and a second peak at about 5 to 8 hours after dosing. There were no differences in pharmacokinetic parameters when this formulation was given with applesauce, but a high fat breakfast may delay absorption time. However, the capsules may be taken with food without clinically significant effects. The Ritalin LA capsule, when opened and sprinkled on a tablespoon of cool applesauce, is bioequivalent to the intact capsule.
Aptensio XR: Aptensio XR follows an extended-release biphasic pharmacokinetic profile to provide day-long medication availability with once daily administration. Aptensio XR capsules contain multilayer beads, which are composed of an immediate-release layer containing approximately 40% of the methylphenidate dose, and a controlled-release layer which contains the remaining 60% of the dose. After oral administration, an initial peak plasma concentration occurs at about 2 hours, with a gradual descending concentration over the next 4 to 6 hours, after which a gradual increase begins reaching a second peak at about 8 hours. The relative bioavailability of Aptensio XR given once daily compared to a methylphenidate immediate-release oral product given 3 times daily in adults is approximately 102%. The pharmacokinetic profile of Aptensio XR administered as a whole capsule or opened and sprinkled onto applesauce under fasting conditions is similar. After a single dose administered to healthy adults under

fasting conditions, the following pharmacokinetic parameters were calculated: Cmax = 23.47 (+/- 11.4) ng/mL, AUC = 258.1 (+/- 94.2) ng x hour/mL, and half-life = 5.09 hours. During pharmacokinetic trials, administration with a high fat meal decreased or diminished the second peak and increased the average Cmax and AUC by 28% and 19%, respectively. At an alcohol concentration up to 40%, there was 96% release of methylphenidate from Aptensio XR capsules within 2 hours; similar results are expected with other capsule strengths.
QuilliChew ER: After a single 40 mg dose under fasting conditions, Cmax was obtained at a median time of 5 hours. Compared to immediate-release chewable tablets (two 20 mg doses given 6 hours apart), methylphenidate mean peak concentration and exposure (AUC) was about 20% and 11% lower, respectively, after a single dose administration of 40 mg QuilliChew ER. Administration with a high-fat meal had no effect on Tmax, and increased Cmax and AUC by about 20% and 4%, respectively, after a single 40 mg dose. Plasma methylphenidate concentrations declined monophasically. The mean elimination half-life was 5.2 hours in healthy volunteers. The presence of alcohol increases release of methylphenidate. At an alcohol concentration up to 40%, there was 90% release of methylphenidate from QuilliChew ER within half an hour; similar results are expected with other available tablet strengths.
Quillivant XR: This extended-release suspension for once-daily administration provides a mean peak plasma concentration of 13.6 +/- 5.8 ng/mL over a median time of 5 hours when given to healthy adults. Food has no clinically significant effect on the bioavailability of the suspension. The relative bioavailability of Quillivant XR compared to immediate-release methylphenidate oral solution is 95%. Elimination half-life is approximately 5 hours.
Cotempla XR-ODT: After a single 51.8 mg dose under fasting conditions, Cmax was obtained at a median time of 5 hours. Compared to an extended-release capsule formulation of methylphenidate, methylphenidate mean peak concentration and exposure (AUC) was about 26% and 6% higher, respectively, after Cotempla XR-ODT administration. Administration with a high-fat meal shorted the median time to peak concentration (Tmax) by 0.5 hours and decreased the Cmax and increased AUC of total methylphenidate by approximately 24% and 16%, respectively. Plasma methylphenidate concentrations declined monophasically. Elimination half-life is approximately 4 hours. The presence of alcohol potentially increases release of methylphenidate. At an alcohol concentration of 40%, an in vitro dissolution study showed alcohol-induced dose dumping potential; dose dumping was not observed with lower alcohol concentrations.
Jornay PM: After a single 100 mg oral dose of Jornay PM administered to healthy adults at 9 PM, the initial absorption of methylphenidate into plasma was delayed such that no more than 5% of total drug was available within the first 10 hours after dosing. After the lag period, the absorption of methylphenidate occurs with a single peak and a median Tmax of 14 hours, followed by a gradual decline throughout the rest of the day. The

relative bioavailability of Jornay PM administered once daily compared to the same daily dose of an oral immediate-release methylphenidate product given 3 times/day in adults is 73.9%. Administration with a high-fat meal at night resulted in a similar mean AUC, a 14% lower mean Cmax, and a median Tmax extended by about 2.5 hours compared to a fasting state. A morning meal has no effect on the kinetics of Jornay PM taken at night. The kinetic parameters of Jornay PM are similar when taken as a whole capsule versus sprinkled on applesauce. The presence of alcohol increases release of methylphenidate in vitro. At an alcohol concentration of 40%, there was a 97% release of methylphenidate from Jornay PM within 2 hours; the increased release rate of methylphenidate was not seen with lower alcohol concentrations.
Adhansia XR: Adhansia XR produces 2 distinct peak concentrations. After Adhansia XR administration, the first median time to Cmax occurs at about 2 (1 to 4) hours and the second at about 10 (8 to 14) hours in pediatric patients 6 to 12 years and 2 (1 to 4) hours for the first and the 11 (8 to 14) hours for the second in pediatric patients 13 to 17 years. The results of pharmacokinetic studies in pediatric patients (6 to 12 years) were comparable to that in adolescents and adults. Elimination half-life is approximately 4 to 7 hours in pediatric patients (6 to 12 years), 5 hours in adolescents, and 7 hours in adults. The AUC and Cmin of d,l-methylphenidate were about 50% and 288% higher, respectively, for Adhansia XR compared to immediate-release methylphenidate at steady state, which was reached on day 3. Administration with a high-fat, high caloric meal did not affect Cmax and AUC. The presence of alcohol increases release of methylphenidate in vitro. At an alcohol concentration of 40%, there was a 71% and 61% faster release of methylphenidate for Adhansia XR 70 mg and 100 mg, respectively, at 2 hours; the increased release rate of methylphenidate was not seen with lower alcohol concentrations. In fasted healthy adults, administration of Adhansia XR 70 mg capsules with 40% alcohol resulted in a 1.4-fold increase in the peak plasma methylphenidate concentration and a 1.3-fold increase in the extent of absorption.

- **Other Route(s)**

Transdermal Route
The extent of methylphenidate systemic absorption after patch administration is dependent on the length of time the patch is worn and the patch size. Peak plasma concentrations of methylphenidate are reached approximately 8 hours after patch application. Cmax and AUC increase significantly with repeated daily administration compared to single-dose administration. After either a 1-day or 7-day patch administration, the Cmax and AUC of d-methylphenidate were approximately 50% lower in adolescents (13 to 17 years of age) than in children (6 to 12 years of age). In clinical pharmacokinetic studies, when the 10 mg/9-hour methylphenidate patch was worn on the hip for 9 hours per day for 4 weeks, the steady state mean d-methylphenidate Cmax was 15.7 +/- 9.39 ng/mL in children 6 years of age and older and 8.32 +/- 4.6 ng/mL in adolescents, and the Cmin was 1.04 +/- 1.17 ng/mL and 0.544 +/- 0.383 ng/mL in children

and adolescents, respectively. In patients who wore the 30 mg/9-hour patch, the mean d-methylphenidate Cmax was 42.9 +/- 22.4 ng/mL in children and 16.5 +/- 6.94 ng/mL in adolescents, and the Cmin was 1.96 +/- 1.73 ng/mL and 1.02 +/- 0.629 ng/mL in children and adolescents, respectively. In children 6 to 12 years of age, mean peak concentrations of transdermal methylphenidate were roughly 1.9 times higher than those observed for once daily oral methylphenidate. However, the Cmax of single dose administration of transdermal methylphenidate is comparable to the Cmax from a single dose of the once daily oral formulations. Transdermal absorption of methylphenidate may increase over time with chronic therapy; these changes cannot be explained by changes in clearance or rate of elimination. On average, steady-state is achieved after approximately 14 days of dosing. The time until any transdermally administered d-methylphenidate is detectable in the circulation averages 3.1 hours (range 1 to 6 hours). The absorption (rate and extent) is increased when methylphenidate patch is applied to inflamed skin or exposed to heat. Absorption characteristics in areas other than the hip are not known.

Once the methylphenidate patch is removed after 9 hours of wear time, methylphenidate plasma concentrations decline in a biexponential manner most likely due to distribution of methylphenidate from the skin after patch removal. The transdermal form of methylphenidate bypasses the liver upon first pass, unlike the oral formulation, resulting in higher serum concentrations with lower initial doses. Results from single- and multiple-dose studies indicate that exposure to l-methylphenidate is 46% of the exposure to d-methylphenidate in children and 40% in adolescents. The pharmacological activity of l-methylphenidate is less than d-methylphenidate. With transdermal administration in children and adolescents, the mean elimination half-life of l-methylphenidate was shorter than for d-methylphenidate and ranged from 1.4 to 2.9 hours; whereas the mean elimination half-life of d-methylphenidate was about 4 to 5 hours.

- **Hepatic Impairment**

There is no experience with methylphenidate in hepatic insufficiency.

- **Renal Impairment**

Since renal clearance is not an important predictor of methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of the drug. However, specific experience in the use of methylphenidate during renal insufficiency is not available.

- **Pediatrics**

In studies with methylphenidate tablets and methylphenidate extended-release capsules (Ritalin LA), the average elimination half-life was about 2.5 hours (range: 1.5 to 5 hours) in children. In general, the Cmax and AUC of d-methylphenidate were

approximately 50% lower in adolescents than in children after administration of the transdermal methylphenidate patch. When a single oral dose of extended-release suspension (Quillivant XR) was given to children (9 to 12 years) and adolescents (13 to 15 years), methylphenidate plasma concentrations in the children were approximately twice those seen in adults, while adolescents had plasma concentrations similar to adults. When a single oral dose of extended-release ODT tablet (Cotempla XR-ODT) was given to children (6 to 12 years) and adolescents (13 to 17 years), methylphenidate plasma concentrations in the children were approximately twice those seen in adults, while adolescents had plasma concentrations similar to adults. In a study of extended-release capsules (Aptensio XR), systemic drug exposures in 4 and 5-year-olds were higher than those in older children and adolescents at the same dose (2 to 3 fold higher Cmax and AUC). The kinetics of a single 54 mg dose of Jornay PM were evaluated in 2 separate studies in adults and in children and adolescents 8 to 17 years of age with ADHD. The qualitative plasma methylphenidate concentration curves and body weight dose-normalized AUC and Cmax were similar between adults, children, and adolescents; however, there were differences in mean kinetic parameters resulting in children being exposed to higher systemic concentrations of methylphenidate than adolescents or adults and adolescents exposed to higher concentrations of methylphenidate than adults when administered the same dose of Jornay PM.

- **Gender Differences**

Plasma concentrations of the major metabolite of methylphenidate appeared to be greater in adult females than in adult males, but no gender differences were observed for methylphenidate plasma concentration in the same subjects. No gender differences have been noted for transdermal methylphenidate.

Administration

For storage information, see the specific product information within the How Supplied section.

Oral Administration

Oral Solid Formulations

Methylin chewable tablets:
Administer 30 to 45 minutes before meals in divided doses 2 to 3 times daily.
Chewable tablets should be taken with at least 8 ounces of fluid to avoid choking.
Do not swallow whole.
Twice-daily dosages may be administered in the morning and around noon.
Individualized timing of the midday dose is usually necessary, as determined by the loss of positive drug effect, which occurs 2 to 6 hours after the morning dose.

Administer the last dose of the day prior to 6 PM.
Immediate-release dosage forms (Ritalin, Methylin, Metadate, generic equivalents):
Administer 30 to 45 minutes before meals in divided doses 2 to 3 times daily.
Twice-daily dosages may be administered in the morning and around noon.
Individualized timing of the midday dose is usually necessary, as determined by the loss of positive drug effect, which occurs 2 to 6 hours after the morning dose.
Administer the last dose of the day prior to 6 PM.
Extended-release tablets (Ritalin SR, Metadate ER, generic methylphenidate ER):
May be administered without regard to meals.
Administer whole; do not cut, crush, or chew.
Extended-release tablets have a duration of action of approximately 8 hours.
Administer the last dose of the day several hours before bedtime.
Once-daily extended-release tablets (Concerta, Relexxii):
Administer once daily in the morning with an adequate amount of fluid.
May be administered without regard to meals.
Administer whole; do not cut, crush, or chew.
The biologically inert portion of this tablet may appear intact in the stool; this is normal.
Once-daily extended-release capsules (Metadate CD, Ritalin LA, Aptensio XR):
May be administered without regard to meals; however, the manufacturer of Aptensio XR recommends that patients establish a routine pattern with regard to meals.
Administer with an adequate amount of fluid.
Do not cut, crush, or chew.
If swallowing is difficult, the capsule may be opened, and the contents gently sprinkled on 1 tablespoon of applesauce and swallowed immediately. The capsule contents (beads) should not be crushed or chewed. Instruct the patient to drink fluids (e.g., water, milk, or juice) after the intake of the sprinkles with applesauce.
The Institute for Safe Medication Practices states the capsule contents of Metadate CD and Ritalin LA may be administered via a nasogastric tube as long as they are not crushed and an adequate amount of fluid is used to wash the full dose down the tube.
Once-daily extended-release chewable tablets (QuilliChew ER):
Administer once daily in the morning with or without food.
The 10 mg and 15 mg doses can be achieved by breaking in half the scored 20 mg and 30 mg tablets, respectively.
Once-daily extended-release orally disintegrating tablets (Cotempla XR-ODT):
Administer once daily in the morning consistently either with or without food.
Do not remove tablet from the blister pack until just prior to dosing; use dry hands when opening the blister pack. Remove the tablet by peeling back the foil; do not push the tablet through the foil.
Place the whole tablet on the tongue and allow it to disintegrate without chewing or crushing.

No liquid is needed to take the tablet.
Once-daily extended-release capsules (Jornay PM):
Administer once daily in the evening consistently either with or without food.
Initiate dosing at 8:00 PM and adjust the timing of administration between 6:30 PM and 9:30 PM to optimize tolerability and efficacy the next morning and throughout the day.
If a dose is missed, advise the patient to take it as soon as it's remembered that same evening. If a patient remembers the missed dose the next morning, skip the dose and do not give until the next scheduled evening administration.
If swallowing is difficult, the capsule may be opened and the contents gently sprinkled on applesauce and swallowed immediately. Do not crush or chew the capsule contents (beads).
Once-daily extended-release capsules (Adhansia XR):
Administer once daily in the morning consistently either with or without food.
Do not cut, crush, or chew.
If swallowing is difficult, the capsule may be opened, and the contents gently sprinkled on 1 tablespoon of applesauce or yogurt and swallowed immediately or within 10 minutes. If not consumed within 10 minutes after mixing, it should be discarded and not stored. The capsule contents (beads) should be taken in its entirety without chewing.
The single dose capsules should not be divided.

Oral Liquid Formulations

Immediate-release oral solution (Methylin):
Measure methylphenidate dosage with an oral syringe or calibrated measuring device.
Administer 30 to 45 minutes before meals in divided doses 2 to 3 times daily. Twice-daily dosages may be administered in the morning and around noon. Individualized timing of the midday dose is usually necessary, as determined by the loss of positive drug effect which occurs 2 to 6 hours after the morning dose. Administer the last dose of the day prior to 6 PM.
Once-daily extended-release oral suspension (Quillivant XR):
Reconstitution
Reconstitute prior to dispensing. Review the manufacturer's reconstitution instructions for the particular product and package size.
Prior to reconstitution, tap the bottle several times to loosen the powder.
To prepare the suspension, add the specified amount of water to the bottle, fully insert the bottle adapter into the bottle neck, replace the cap, and vigorously shake the bottle for at least 10 seconds.
Storage: Store reconstituted suspension at 77 degrees F; dispense in original packaging (bottle in carton). The reconstituted suspension is stable for 4 months from date of reconstitution.
Administration
Vigorously shake the bottle of suspension for a minimum of 10 seconds before each

use.
Measure dosage with the calibrated oral dosing dispenser provided.
Administer in the morning without regard to meals.

Topical Administration

Transdermal Patch Formulations

Daytrana transdermal system:
Patch should be applied 2 hours before the effect is needed.
Do not cut or trim patch.
Apply patch immediately after opening the pouch and removing protective liner. Do not use if pouch seal is broken. Do not touch the adhesive side of the patch during application to avoid absorption of methylphenidate. Wash hands immediately if adhesive side of the patch is touched. Discard the patch if difficulty is encountered in separating the patch from the release liner, or if tearing or other damage occurs. Discard patch if adhesive containing medication has transferred to the liner during removal of the patch from the liner.
Place on a dry, clean area of the hip and hold in place for 30 seconds with the palm of the hand. Do not apply to oily, damaged, or irritated skin. Do not apply topical preparations to the application site immediately prior to patch application. Avoid the waistline area where the patch could be rubbed by clothing.
Applications sites should be alternated from one hip to the next each day, avoiding sites where a patch was recently placed, when possible.
Instruct patient on proper application and disposal of patch. Adherence of the patch may be affected by showering, bathing, or swimming. The carton contains an administration chart that can help the patient monitor application and removal time, which the patient and/or caregiver should be encouraged to use. If a patch was removed without the caregiver's knowledge, or if a patch is missing from the tray, the caregiver should be encouraged to ask the child when and how the patch was removed.
Avoid exposing the application site to hair dryers, heating pads, electric blankets, heated water beds, or other direct external heat sources. The rate and extent of absorption of methylphenidate are significantly increased during application of heat to the patch during use. Temperature-dependent increases in absorption may be greater than 2-fold, potentially resulting in overdose.
Do not apply or re-apply the patch with dressings, tape, or adhesives. If the patch is not fully adhered to the skin during application or wear time, discard the patch according to disposal instructions and apply a new patch.
The total daily wear time should not exceed 9 hours, regardless of patch replacement.
Patches should be peeled off slowly. Patch removal may be aided by applying an oil-based product (i.e., petroleum jelly, mineral oil, olive oil) to the patch edges and gently working the oil underneath the edges of the patch.

Disposal: Instruct patient and/or caregiver to fold used patches, so that the adhesive side of the patch adheres to itself, and then flush it down the toilet or dispose of in an appropriate lidded container. If the patient stops using the prescription, each unused patch should be removed from its pouch, separated from the protective liner, folded onto itself, and flushed down the toilet or disposed of in an appropriate lidded container. Do not flush pouch and protective liner down the toilet. Instead, dispose of them in an appropriate container with a lid.

Maximum Dosage Limits

- **Adults**
  100 mg/day PO for Adhansia XR; 72 mg/day PO for Concerta and Relexxii; 60 mg/day PO for all other oral formulations.
- **Geriatric**
  100 mg/day PO for Adhansia XR; 60 mg/day PO for all other oral formulations. While some dosage forms have not been specifically studied in the elderly, use of stimulants off-label has been described in geriatric adults.
- **Adolescents**
  85 mg/day PO for Adhansia XR; 72 mg/day (Max: 2 mg/kg/day) PO for Concerta and Relexxii (FDA-approved labeling); 60 mg/day PO for all other oral formulations excluding Cotempla XR-ODT and Jornay PM (FDA-approved labeling); 51.8 mg/day PO for Cotempla XR-ODT and 100 mg/day PO for Jornay PM; however, doses up to 100 to 108 mg/day PO have been used in patients weighing more than 50 kg for some formulations. For the transdermal patch, 30 mg/9-hour patch per day is the maximum.
- **Children**
  6 to 12 years: 85 mg/day PO for Adhansia XR; 54 mg/day PO for Concerta and Relexxii (FDA-approved labeling); 60 mg/day PO for all other oral formulations excluding Cotempla XR-ODT and Jornay PM (FDA-approved labeling); 51.8 mg/day PO for Cotempla XR-ODT and 100 mg/day PO for Jornay PM; however, doses up to 100 to 108 mg/day PO have been used in patients weighing more than 50 kg for some formulations. For the transdermal patch, 30 mg/9-hour patch per day is the maximum.
  3 to 5 years: Safety and efficacy have not been established. Maximum doses have not been adequately studied; however, the Preschool ADHD Treatment Study (PATS) has suggested immediate-release doses up to 30 mg/day PO.
  1 to 2 years: Safety and efficacy have not been established.
- **Infants**
  Safety and efficacy have not been established.

- **Neonates**
  Safety and efficacy have not been established.

Dosage Forms

- Adhansia XR 35mg Extended-Release Capsule
- Aptensio XR 10mg Extended-Release Capsule
- Aptensio XR 15mg Extended-Release Capsule
- Aptensio XR 20mg Extended-Release Capsule
- Aptensio XR 30mg Extended-Release Capsule
- Aptensio XR 40mg Extended-Release Capsule
- Aptensio XR 50mg Extended-Release Capsule
- Aptensio XR 60mg Extended-Release Capsule
- Concerta 18mg Extended-Release Tablet
- Concerta 27mg Extended-Release Tablet
- Concerta 36mg Extended-Release Tablet
- Concerta 54mg Extended-Release Tablet
- Cotempla XR-ODT 17.3mg Extended-Release Orally Disintegrating Tablet
- Cotempla XR-ODT 25.9mg Extended-Release Orally Disintegrating Tablet
- Cotempla XR-ODT 8.6mg Extended-Release Orally Disintegrating Tablet
- Daytrana 10mg/9hr Transdermal System
- Daytrana 15mg/9hr Transdermal System
- Daytrana 20mg/9hr Transdermal System
- Daytrana 30mg/9hr Transdermal System
- Jornay PM 100mg Extended-Release Capsule
- Jornay PM 20mg Extended-Release Capsule
- Jornay PM 40mg Extended-Release Capsule
- Jornay PM 60mg Extended-Release Capsule
- Jornay PM 80mg Extended-Release Capsule
- Metadate CD 10mg Extended-Release Capsule
- Metadate CD 20mg Extended-Release Capsule
- Metadate CD 30mg Extended-Release Capsule
- Metadate CD 40mg Extended-Release Capsule
- Metadate CD 50mg Extended-Release Capsule
- Metadate CD 60mg Extended-Release Capsule
- Methylin 10mg/5ml Solution
- Methylin 5mg/5ml Solution
- Methylphenidate Hydrochloride 1.1mg/1h Transdermal Patch - 9 hour
- Methylphenidate Hydrochloride 1.6mg/1h Transdermal Patch - 9 hour
- Methylphenidate Hydrochloride 10mg Chewable tablet

- Methylphenidate Hydrochloride 10mg Oral capsule, 30/70 biphasic release
- Methylphenidate Hydrochloride 10mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 10mg Oral capsule, 50/50 biphasic release
- Methylphenidate Hydrochloride 10mg Oral capsule, biphasic release
- Methylphenidate Hydrochloride 10mg Oral tablet
- Methylphenidate Hydrochloride 10mg Oral tablet, extended release
- Methylphenidate Hydrochloride 10mg/5mL Oral solution
- Methylphenidate Hydrochloride 15mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 18mg Oral tablet, extended release
- Methylphenidate Hydrochloride 2.2mg/1h Transdermal Patch - 9 hour
- Methylphenidate Hydrochloride 2.5mg Chewable tablet
- Methylphenidate Hydrochloride 20mg Oral capsule, 30/70 biphasic release
- Methylphenidate Hydrochloride 20mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 20mg Oral capsule, 50/50 biphasic release
- Methylphenidate Hydrochloride 20mg Oral capsule, biphasic release
- Methylphenidate Hydrochloride 20mg Oral tablet
- Methylphenidate Hydrochloride 20mg Oral tablet, extended release
- Methylphenidate Hydrochloride 27mg Oral tablet, extended release
- Methylphenidate Hydrochloride 3.3mg/1h Transdermal Patch - 9 hour
- Methylphenidate Hydrochloride 30mg Oral capsule, 30/70 biphasic release
- Methylphenidate Hydrochloride 30mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 30mg Oral capsule, 50/50 biphasic release
- Methylphenidate Hydrochloride 30mg Oral capsule, biphasic release
- Methylphenidate Hydrochloride 36mg Oral tablet, extended release
- Methylphenidate Hydrochloride 40mg Oral capsule, 30/70 biphasic release
- Methylphenidate Hydrochloride 40mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 40mg Oral capsule, 50/50 biphasic release
- Methylphenidate Hydrochloride 40mg Oral capsule, biphasic release
- Methylphenidate Hydrochloride 45mg Oral tablet, extended release
- Methylphenidate Hydrochloride 50mg Oral capsule, 30/70 biphasic release
- Methylphenidate Hydrochloride 50mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 54mg Oral tablet, extended release
- Methylphenidate Hydrochloride 5mg Chewable tablet
- Methylphenidate Hydrochloride 5mg Oral tablet
- Methylphenidate Hydrochloride 5mg/5mL Oral solution
- Methylphenidate Hydrochloride 60mg Oral capsule, 30/70 biphasic release
- Methylphenidate Hydrochloride 60mg Oral capsule, 40/60 biphasic release
- Methylphenidate Hydrochloride 60mg Oral capsule, 50/50 biphasic release
- Methylphenidate Hydrochloride 63mg Oral tablet, extended release
- Methylphenidate Hydrochloride 72mg Oral tablet, extended release

- Methylphenidate Hydrochloride Bulk powder
- QuilliChew ER 20mg Extended-Release Chewable Tablet
- QuilliChew ER 30mg Extended-Release Chewable Tablet
- QuilliChew ER 40mg Extended-Release Chewable Tablet
- Quillivant XR 300mg/60mL Powder for Suspension
- Quillivant XR 600mg/120mL Powder for Suspension
- Quillivant XR 750mg/150mL Powder for Suspension
- Quillivant XR 900mg/180mL Powder for Suspension
- RELEXXII 18mg Extended-Release Tablet
- RELEXXII 27mg Extended-Release Tablet
- RELEXXII 36mg Extended-Release Tablet
- RELEXXII 45mg Extended-Release Tablet
- RELEXXII 54mg Extended-Release Tablet
- RELEXXII 63mg Extended-Release Tablet
- RELEXXII 72mg Extended-Release Tablet
- Ritalin 10mg Tablet
- Ritalin 20mg Tablet
- Ritalin 5mg Tablet
- Ritalin LA 10mg Extended-Release Capsule
- Ritalin LA 20mg Extended-Release Capsule
- Ritalin LA 30mg Extended-Release Capsule
- Ritalin LA 40mg Extended-Release Capsule

Dosage Adjustment Guidelines

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available.

Renal Impairment

Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed. Renal clearance is not an important predictor of methylphenidate clearance.