

## Drug Information Provided by Elsevier

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## Brand Names

Xyzal, Xyzal Allergy 24 Hour, Xyzal Children's Allergy 24 Hour, Xyzal Solution

## Indication Specific Dosing

**For the management of symptoms of seasonal allergies or perennial allergies, including allergic rhinitis**

### Oral dosage (solution)

#### Adults

2.5 or 5 mg PO once daily in the evening. Some, such as those with less severe symptoms, experience adequate symptom control with 2.5 mg/day. For geriatric adults, prescription labeling recommends starting with 2.5 mg/day.

#### Children and Adolescents 12 to 17 years

2.5 or 5 mg PO once daily in the evening. Some, such as those with less severe symptoms, experience adequate symptom control with 2.5 mg/day.

#### Children 6 to 11 years

2.5 mg PO once daily in the evening.

#### Children 2 to 5 years

1.25 mg PO once daily in the evening.

#### Infants and Children 6 months to 1 year

1.25 mg PO once daily in the evening. Use by prescription only.

### Oral dosage (tablet)

#### Adults

5 mg PO once daily in the evening. Some, such as those with less severe symptoms, experience adequate symptom control with 2.5 mg/day. For geriatric adults, prescription labeling recommends starting with 2.5 mg/day.

### **Children and Adolescents 12 to 17 years**

5 mg PO once daily in the evening. Some, such as those with less severe symptoms, experience adequate symptom control with 2.5 mg/day.

### **Children 6 to 11 years**

2.5 mg PO once daily in the evening.

## **For the treatment of chronic spontaneous urticaria (chronic idiopathic urticaria)**

### **Oral dosage (solution)**

#### **Infants and Children 6 months to 5 years**

1.25 mg PO once daily in the evening.

### **Oral dosage (tablet and solution)**

#### **Adults**

5 mg PO once daily in the evening. Some patients may be adequately controlled by 2.5 mg/day in the evening. In geriatric adults, use an initial dose of 2.5 mg/day.

### **Children and Adolescents 12 years and older**

5 mg PO once daily in the evening. Some patients may be adequately controlled by 2.5 mg/day in the evening.

### **Children 6 to 11 years**

2.5 mg PO once daily in the evening.

## **For the symptomatic treatment of atopic dermatitis**

### **Oral dosage (solution)**

#### **Children 1 to 2 years**

0.125 mg/kg/dose PO twice daily. Total daily dosage range from clinical studies: 2.83 to 3.83 mg/day.

## Contraindications And Precaution

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### 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. Levocetirizine is contraindicated for use in patients with a cetirizine or hydroxyzine hypersensitivity. Cetirizine is a known human metabolite of hydroxyzine, and levocetirizine is an enantiomer of cetirizine.

### **renal failure, renal impairment**

Do not use non-prescription (OTC) levocetirizine products in people with renal impairment without care team approval due to the need for dosage adjustment.

Levocetirizine prescription products are contraindicated for use in pediatric patients less than 12 years of age with any degree of renal impairment. Levocetirizine is also contraindicated in all patients with end-stage renal failure (CrCl less than 10 mL/minute) and patients receiving dialysis. Dosage adjustments are required for adults, adolescents, and children less than 12 years of age with mild (CrCl 50 to 80 mL/minute), moderate (CrCl 30 to 50 mL/minute), or severe renal impairment (CrCl 10 to 30 mL/minute). Renal excretion is the primary route of levocetirizine elimination and renal clearance of the drug correlates with creatinine clearance.

### **activities requiring coordination and concentration, driving or operating machinery**

Drowsiness has been reported in some levocetirizine recipients. Treated patients should use caution when driving or operating machinery or with other activities requiring coordination and concentration until the effects of the drug are known. Concurrent use of alcohol or other CNS depressants may increase drowsiness.

### **prostatic hypertrophy, urinary retention**

Levocetirizine should be used with caution in patients with predisposing factors of

urinary retention (e.g., spinal cord lesion, prostatic hypertrophy) as levocetirizine may increase the risk of urinary retention. People with a history of urinary retention or problems with emptying their bladder should consult their care team before nonprescription use of levocetirizine. If trouble urinating occurs during treatment, patients should stop use of levocetirizine and consult their health care provider.

## **pregnancy**

Levocetirizine may be used during pregnancy. In animal reproduction studies, there was no evidence of fetal harm with the administration of levocetirizine during organogenesis at doses greatly exceeding the maximum recommended human dose (MRHD) in adults (doses up to 390 and 470 times, respectively, in pregnant rats and rabbits). Pregnant individuals should seek health care professional advice before use of nonprescription (OTC) products. Levocetirizine is the active, R-enantiomer of cetirizine and is generally considered to be acceptable to use during pregnancy based on the available data with cetirizine use during pregnancy. Oral cetirizine and loratadine are considered acceptable antihistamine alternatives for the treatment of allergies and urticaria based on their excellent safety data and recommendation in multiple guidelines for use during pregnancy.

## **breast-feeding**

Levocetirizine may be used during breast-feeding. Published data indicate that transfer of levocetirizine (R-enantiomer of cetirizine) and the parent drug cetirizine into human breast milk is low and therefore adverse effects are not expected in breastfed infants. Because of its lack of sedation and low milk concentrations, loratadine is also not expected to cause adverse effects in breastfed infants and is usually considered compatible with breast-feeding. Some guidelines also recommend loratadine or cetirizine at the lowest dose as preferred antihistamines in individuals who are breast-feeding.

## **Pregnancy And Lactation**

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Levocetirizine may be used during pregnancy. In animal reproduction studies, there was no evidence of fetal harm with the administration of levocetirizine during organogenesis at doses greatly exceeding the maximum recommended human dose (MRHD) in adults (doses up to 390 and 470 times, respectively, in pregnant rats and rabbits). Pregnant individuals should seek health care professional advice before use of nonprescription (OTC) products. Levocetirizine is the active, R-enantiomer of cetirizine and is generally considered to be acceptable to use during pregnancy based on the available data with

cetirizine use during pregnancy. Oral cetirizine and loratadine are considered acceptable antihistamine alternatives for the treatment of allergies and urticaria based on their excellent safety data and recommendation in multiple guidelines for use during pregnancy.

## Interactions

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Acetaminophen; Aspirin; diphenhydramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Caffeine; Dihydrocodeine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Acetaminophen; Caffeine; Pyrilamine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Chlorpheniramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Chlorpheniramine; Dextromethorphan: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Chlorpheniramine; Phenylephrine : (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during

coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; Codeine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Acetaminophen; Dextromethorphan; Doxylamine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; diphenhydramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Acetaminophen; HYDROcodone: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Acetaminophen; oxyCODONE: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Acetaminophen; Pamabrom; Pyrilamine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

ALFentanil: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the

minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

**ALPRAZolam:** (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**Amitriptyline:** (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

**Amobarbital:** (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**Amoxapine:** (Moderate) Concurrent use of cetirizine/levocetirizine with heterocyclic antidepressants should generally be avoided. Coadministration may increase the risk of anticholinergic and CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive anticholinergic effects, sedation, and somnolence.

**Apomorphine:** (Moderate) Concurrent use of cetirizine/levocetirizine with apomorphine should generally be avoided because of the possibility of additive sedative effects.

Dopaminergic agents have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment.

**ARIPIPRAZOLE:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

**Asenapine:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

**Aspirin, ASA; Butalbital; Caffeine:** (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**Aspirin, ASA; Caffeine; Orphenadrine:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the

risk for additive CNS depression.

Aspirin, ASA; Carisoprodol; Codeine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Aspirin, ASA; oxyCODONE: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Atropine: (Moderate) Monitor for unusual drowsiness or excess sedation and for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and atropine use. Concomitant use may result in additive CNS depression or anticholinergic adverse effects.

Atropine; Difenoxin: (Moderate) Concurrent administration of diphenoxylate/difenoxin with cetirizine can potentiate the CNS-depressant effects of diphenoxylate/difenoxin. Use caution during coadministration. (Moderate) Monitor for unusual drowsiness or excess sedation and for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and atropine use. Concomitant use may result in additive CNS depression or anticholinergic adverse effects.

atypical antipsychotic: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Baclofen: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Barbiturates: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Belladonna; Opium: (Major) Reserve concomitant use of opioids and cetirizine for

patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and belladonna use. Concomitant use may result in additive anticholinergic adverse effects.

Benzhydrocodone; Acetaminophen: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Benzodiazepines: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and hyoscyamine use. Concomitant use may result in additive anticholinergic adverse effects.

Benztropine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and bentsropine use. Concomitant use may result in additive anticholinergic adverse effects.

Brexpiprazole: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Brompheniramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Brompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Brompheniramine; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Brompheniramine; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Brompheniramine; Pseudoephedrine; Dextromethorphan: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Budesonide; Glycopyrrolate; Formoterol: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use.

Concomitant use may result in additive anticholinergic adverse effects.

Buprenorphine: (Major) Reserve concomitant use of buprenorphine and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Buprenorphine; Naloxone: (Major) Reserve concomitant use of buprenorphine and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Butalbital; Acetaminophen: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Butalbital; Acetaminophen; Caffeine: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Butalbital; Acetaminophen; Caffeine; Codeine: (Major) Reserve concomitant use of

opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Butalbital; Aspirin; Caffeine; Codeine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Butorphanol: (Moderate) Concurrent use of cetirizine/levocetirizine with butorphanol should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Calcium, Magnesium, Potassium, Sodium Oxybates: (Moderate) Concurrent use of cetirizine/levocetirizine with sodium oxybate should generally be avoided.

Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Cannabidiol: (Moderate) Concurrent use of cetirizine with cannabidiol should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Capsaicin; Metaxalone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Carbidopa; Levodopa; Entacapone: (Moderate) Caution is recommended during concurrent use of cetirizine or levocetirizine with COMT inhibitors because of the possibility for additive sedative effects. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or

sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.

Carbinoxamine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Cariprazine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Carisoprodol: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Celecoxib; Tramadol: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Cenobamate: (Moderate) Monitor for excessive sedation and somnolence during coadministration of cenobamate and cetirizine. Concurrent use may result in additive CNS depression.

Chlophedianol; Dexbrompheniramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorcyclizine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

chlordiazepoxide: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

chlordiazepoxide; Amitriptyline: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence. (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

chlordiazepoxide; Clidinium: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Chlorpheniramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Codeine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Dextromethorphan: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; HYDROcodone: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit

dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorpheniramine; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Chlorzoxazone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Clemastine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

clomiPRAMINE: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

clonazePAM: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

cloNIDine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and clonidine due to the risk for additive CNS depression.

Clorazepate: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-

related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**cloZAPine:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

**Codeine:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

**Codeine; Dexbrompheniramine:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

**Codeine; guaiFENesin:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

**Codeine; guaiFENesin; Pseudoephedrine:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Codeine; Phenylephrine; Promethazine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Codeine; Promethazine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

COMT inhibitors: (Moderate) Caution is recommended during concurrent use of cetirizine or levocetirizine with COMT inhibitors because of the possibility for additive sedative effects. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.

Cyclobenzaprine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Cyproheptadine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Dantrolene: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Desipramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

Desloratadine: (Minor) Although desloratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be

prudent to monitor for drowsiness during concurrent use of desloratadine with CNS depressants such as other H1-blockers.

Desloratadine; Pseudoephedrine: (Minor) Although desloratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of desloratadine with CNS depressants such as other H1-blockers.

Deutetrabenazine: (Moderate) Concurrent use of cetirizine/levocetirizine with deutetrabenazine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Dexbrompheniramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Dexbrompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Dexbrompheniramine; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Dexchlorpheniramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

dexmedeTOMIDine: (Moderate) Concurrent use of cetirizine/levocetirizine with dexmedetomidine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of dexmedetomidine; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

Dextromethorphan; diphenhydrAMINE; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

diazepam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines

should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Dicyclomine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and dicyclomine use. Concomitant use may result in additive anticholinergic adverse effects.

dimenhyDRINATE: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

diphenhydrAMINE: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

diphenhydrAMINE; Ibuprofen: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

diphenhydrAMINE; Naproxen: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

diphenhydrAMINE; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Diphenoxylate; Atropine: (Moderate) Concurrent administration of diphenoxylate/difenoxin with cetirizine can potentiate the CNS-depressant effects of diphenoxylate/difenoxin. Use caution during coadministration. (Moderate) Monitor for unusual drowsiness or excess sedation and for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and atropine use. Concomitant use may result in additive CNS depression or anticholinergic adverse effects.

Doxepin: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

Doxylamine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Doxylamine; Pyridoxine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

droNABinol: (Moderate) Additive drowsiness may occur if cetirizine/levocetirizine is administered with other drugs that depress the CNS, including dronabinol.

droPERidol: (Moderate) Concurrent use of cetirizine/levocetirizine with droperidol should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Entacapone: (Moderate) Caution is recommended during concurrent use of cetirizine or levocetirizine with COMT inhibitors because of the possibility for additive sedative effects. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.

Esketamine: (Moderate) Closely monitor patients receiving esketamine and cetirizine for sedation and other CNS depressant effects. Instruct patients who receive a dose of esketamine not to drive or engage in other activities requiring alertness until the next day after a restful sleep.

Estazolam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Eszopiclone: (Moderate) Concurrent use of cetirizine/levocetirizine with eszopiclone should generally be avoided. Concurrent use of eszopiclone with other CNS depressants increases the risk for CNS depression and complex sleep-related behaviors (e.g., driving, talking, eating, or performing other activities while not fully awake). If concurrent use is necessary, patients should be instructed to contact their provider immediately if these symptoms or behaviors occur.

Etomidate: (Moderate) Concurrent use of cetirizine/levocetirizine with general anesthetics should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of general anesthetics; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

Fenfluramine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of fenfluramine and cetirizine. Concurrent use may result in additive CNS depression.

fentaNYL: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

flavoxATE: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and flavoxate use. Concomitant use may result in additive anticholinergic adverse effects.

Flibanserin: (Moderate) Concurrent use of cetirizine/levocetirizine with flibanserin should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Flurazepam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Gabapentin: (Moderate) Monitor for respiratory depression and sedation during concomitant cetirizine and gabapentin use; consider starting gabapentin at a low dose. Concomitant use increases the risk for additive CNS depression.

General anesthetics: (Moderate) Concurrent use of cetirizine/levocetirizine with general anesthetics should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of general anesthetics; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

Glycopyrrolate: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.

Glycopyrrolate; Formoterol: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.

guanFACINE: (Moderate) Concurrent use of cetirizine/levocetirizine with guanfacine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Haloperidol: (Moderate) Concurrent use of cetirizine/levocetirizine with haloperidol should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and

somnolence.

Heparin: (Minor) Antihistamines may partially counteract the anticoagulant actions of heparin, according to the product labels. However, this interaction is not likely of clinical significance since heparin therapy is adjusted to the partial thromboplastin time (aPTT) and other clinical parameters of the patient.

Heterocyclic antidepressants: (Moderate) Concurrent use of cetirizine/levocetirizine with heterocyclic antidepressants should generally be avoided. Coadministration may increase the risk of anticholinergic and CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive anticholinergic effects, sedation, and somnolence.

Homatropine; HYDROcodone: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

(Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and homatropine use. Concomitant use may result in additive anticholinergic adverse effects.

HYDROcodone: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

HYDROcodone; Ibuprofen: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

HYDROmorphine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and

sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

hydROXYzine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Hyoscyamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and hyoscyamine use. Concomitant use may result in additive anticholinergic adverse effects.

Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and hyoscyamine use. Concomitant use may result in additive anticholinergic adverse effects.

Iloperidone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Imipramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

Indacaterol; Glycopyrrolate: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.

Isocarboxazid: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and monoamine oxidase inhibitors (MAOIs). Concomitant use may result in additive CNS depression or anticholinergic effects.

Isoflurane: (Moderate) Concurrent use of cetirizine/levocetirizine with general anesthetics should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of general anesthetics; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

Ketamine: (Moderate) Concurrent use of cetirizine/levocetirizine with general anesthetics should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of general anesthetics; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

Lemborexant: (Moderate) Monitor for excessive sedation and somnolence during coadministration of lemborexant and cetirizine. Dosage adjustments of lemborexant and cetirizine may be necessary when administered together because of potentially additive CNS effects. The risk of next-day impairment, including impaired driving, is increased if lemborexant is taken with other CNS depressants.

Levorphanol: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Lofexidine: (Moderate) Concurrent use of cetirizine/levocetirizine with lofexidine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Lopinavir; Ritonavir: (Moderate) Coadministration of cetirizine and ritonavir resulted in a 42% increase in the AUC, 53% increase in half-life, and 29% decrease in clearance of cetirizine. Cetirizine did not alter ritonavir disposition.

Loratadine: (Minor) Although loratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of loratadine with CNS depressants such as other H1-blockers.

Loratadine; Pseudoephedrine: (Minor) Although loratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of loratadine with CNS depressants such as other H1-blockers.

LORazepam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Loxapine: (Moderate) Concurrent use of cetirizine/levocetirizine with loxapine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Lumateperone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Lurasidone: (Moderate) Monitor for unusual drowsiness and sedation during

coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Maprotiline: (Moderate) Concurrent use of cetirizine/levocetirizine with heterocyclic antidepressants should generally be avoided. Coadministration may increase the risk of anticholinergic and CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive anticholinergic effects, sedation, and somnolence.

Meclizine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Melatonin: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and melatonin due to the risk for additive CNS depression.

Meperidine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Meprobamate: (Moderate) Concurrent use of cetirizine/levocetirizine with meprobamate should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Metaxalone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Methadone: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and hyoscyamine use. Concomitant use may result in additive anticholinergic adverse effects.

Methohexital: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates

should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Methscopolamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and methscopolamine use. Concomitant use may result in additive anticholinergic adverse effects.

Methyldopa: (Moderate) Concurrent use of cetirizine/levocetirizine with methyldopa should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Midazolam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Mirtazapine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and mirtazapine due to the risk for additive CNS depression.

Molindone: (Moderate) Concurrent use of cetirizine/levocetirizine with molindone should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Monoamine oxidase inhibitors: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and monoamine oxidase inhibitors (MAOIs). Concomitant use may result in additive CNS depression or anticholinergic effects.

Morphine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Nalbuphine: (Moderate) Concurrent use of cetirizine/levocetirizine with nalbuphine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Nefazodone: (Moderate) Concurrent use of cetirizine/levocetirizine with nefazodone should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and

somnolence.

Neostigmine; Glycopyrrolate: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.

Nirmatrelvir; Ritonavir: (Moderate) Coadministration of cetirizine and ritonavir resulted in a 42% increase in the AUC, 53% increase in half-life, and 29% decrease in clearance of cetirizine. Cetirizine did not alter ritonavir disposition.

Nortriptyline: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

OLANZapine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

OLANZapine; FLUoxetine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

OLANZapine; Samidorphan: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Oliceridine: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Opiate Agonists: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Opicapone: (Moderate) Caution is recommended during concurrent use of cetirizine or levocetirizine with COMT inhibitors because of the possibility for additive sedative effects. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases.

Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.

Orphenadrine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

Oxazepam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

oxyBUTYNIN: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and oxybutynin use. Concomitant use may result in additive anticholinergic adverse effects.

oxyCODONE: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

oxyMORPHONE: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Paliperidone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Pentazocine; Naloxone: (Moderate) Concurrent use of cetirizine/levocetirizine with pentazocine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

PENTobarbital: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and

somnolence.

Perampanel: (Moderate) Concurrent use of cetirizine/levocetirizine with perampanel should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Perphenazine; Amitriptyline: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

Phenelzine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and monoamine oxidase inhibitors (MAOIs). Concomitant use may result in additive CNS depression or anticholinergic effects.

PHENobarbital: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and hyoscyamine use. Concomitant use may result in additive anticholinergic adverse effects. (Moderate) Monitor for unusual drowsiness or excess sedation and for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and atropine use. Concomitant use may result in additive CNS depression or anticholinergic adverse effects. (Moderate) Monitor for unusual drowsiness or excess sedation and for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and scopolamine use. Concomitant use may result in additive CNS depression or anticholinergic adverse effects.

Pimavanserin: (Moderate) Concurrent use of cetirizine/levocetirizine with pimavanserin should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Pimozide: (Moderate) Concurrent use of cetirizine/levocetirizine with pimozide should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Pramipexole: (Moderate) Concurrent use of cetirizine/levocetirizine with pramipexole should generally be avoided because of the possibility of additive sedative effects.

Dopaminergic agents have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment.

Pregabalin: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and pregabalin due to the risk for additive CNS depression.

Primidone: (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Propantheline: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and propantheline use. Concomitant use may result in additive anticholinergic adverse effects.

Propofol: (Moderate) Concurrent use of cetirizine/levocetirizine with general anesthetics should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of general anesthetics; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

Protriptyline: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

Pseudoephedrine; Triprolidine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Quazepam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

QUEtiapine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Ramelteon: (Moderate) Concurrent use of cetirizine/levocetirizine with ramelteon should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Rasagiline: (Moderate) Concurrent use of cetirizine/levocetirizine with rasagiline should generally be avoided because of the possibility of additive sedative effects.

Dopaminergic agents have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment.

**Remifentanil:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

**Remimazolam:** (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**risperiDONE:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

**Ritonavir:** (Moderate) Coadministration of cetirizine and ritonavir resulted in a 42% increase in the AUC, 53% increase in half-life, and 29% decrease in clearance of cetirizine. Cetirizine did not alter ritonavir disposition.

**rOPINIRole:** (Moderate) Concurrent use of cetirizine/levocetirizine with ropinirole should generally be avoided because of the possibility of additive sedative effects.

Dopaminergic agents have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment.

**Rotigotine:** (Moderate) Concurrent use of cetirizine/levocetirizine with rotigotine should generally be avoided because of the possibility of additive sedative effects.

Dopaminergic agents have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment.

**Safinamide:** (Moderate) Concurrent use of cetirizine/levocetirizine with safinamide should generally be avoided because of the possibility of additive sedative effects.

Dopaminergic agents have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment.

**Scopolamine:** (Moderate) Monitor for unusual drowsiness or excess sedation and for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and scopolamine use. Concomitant use may result in additive CNS depression or anticholinergic adverse effects.

**Secobarbital:** (Moderate) Concurrent use of cetirizine/levocetirizine with barbiturates should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**Sedating H1-blockers:** (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

**Selegiline:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and selegiline due to the risk for additive CNS depression.

**Sevoflurane:** (Moderate) Concurrent use of cetirizine/levocetirizine with general anesthetics should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. CNS depression is a desired effect of general anesthetics; however, concurrent use with a CNS depressant may prolong recovery. If concurrent use is necessary, monitor patients closely.

**Sincalide:** (Moderate) Sincalide-induced gallbladder ejection fraction may be affected by concurrent medications, including H1-blockers. False study results are possible; thorough patient history is important in the interpretation of procedure results.

**Skeletal Muscle Relaxants:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and skeletal muscle relaxants due to the risk for additive CNS depression.

**Sodium Oxybate:** (Moderate) Concurrent use of cetirizine/levocetirizine with sodium oxybate should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**Stiripentol:** (Moderate) Concurrent use of cetirizine/levocetirizine with stiripentol should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**SUFentanil:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention

and/or severe constipation, which may lead to paralytic ileus.

Suvorexant: (Moderate) Concurrent use of cetirizine/levocetirizine with suvorexant should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Tapentadol: (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

Tasimelteon: (Moderate) Concurrent use of cetirizine/levocetirizine with tasimelteon should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Temazepam: (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Tetrabenazine: (Moderate) Concurrent use of cetirizine/levocetirizine with tetrabenazine should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Thalidomide: (Moderate) Concurrent use of cetirizine/levocetirizine with thalidomide should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Theophylline, Aminophylline: (Minor) Large doses of aminophylline may reduce the clearance of cetirizine/levocetirizine. Monitor the patient clinically for an altered response to cetirizine/levocetirizine if coadministered with aminophylline. (Minor) Large doses of theophylline may reduce the clearance of cetirizine/levocetirizine. Monitor the patient clinically for increased cetirizine/levocetirizine-related adverse effects if coadministered with theophylline.

Thiothixene: (Moderate) Concurrent use of cetirizine/levocetirizine with thiothixene should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Tolcapone: (Moderate) Caution is recommended during concurrent use of cetirizine or

levocetirizine with COMT inhibitors because of the possibility for additive sedative effects. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.

**traMADol:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

**Tramadol; Acetaminophen:** (Major) Reserve concomitant use of opioids and cetirizine for patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose and monitor for signs of urinary retention or reduced gastric motility. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death as well as urinary retention and/or severe constipation, which may lead to paralytic ileus.

**Tranylcypromine:** (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and monoamine oxidase inhibitors (MAOIs). Concomitant use may result in additive CNS depression or anticholinergic effects.

**traZODone:** (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and trazodone due to the risk for additive CNS depression.

**Triazolam:** (Moderate) Concurrent use of cetirizine/levocetirizine with benzodiazepines should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

**Tricyclic antidepressants:** (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

**Trihexyphenidyl:** (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and trihexyphenidyl use. Concomitant use may result in additive anticholinergic adverse effects.

Trimipramine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and tricyclic antidepressants. Concomitant use may result in additive CNS depression or anticholinergic effects.

Triprolidine: (Moderate) Monitor for unusual drowsiness and sedation, urinary retention, and reduced gastric motility during coadministration of cetirizine and sedating H1-blockers. Concomitant use may result in additive CNS depression or anticholinergic effects.

Trospium: (Moderate) Dry mouth and drowsiness may occur in patients receiving cetirizine/levocetirizine; caution may be necessary during concomitant use of cetirizine/levocetirizine with the antimuscarinics.

Valerian, Valeriana officinalis: (Moderate) Concurrent use of cetirizine/levocetirizine with valerian should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Valproic Acid, Divalproex Sodium: (Moderate) Concurrent use of cetirizine/levocetirizine with valproic acid should generally be avoided. Coadministration may increase the risk of CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive sedation and somnolence.

Xanomeline; Trospium: (Moderate) Dry mouth and drowsiness may occur in patients receiving cetirizine/levocetirizine; caution may be necessary during concomitant use of cetirizine/levocetirizine with the antimuscarinics.

Zaleplon: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and zaleplon due to the risk for additive CNS depression and next-day psychomotor impairment; dose adjustments may be necessary.

Ziprasidone: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of atypical antipsychotics and cetirizine due to the risk for additive CNS depression.

Zolpidem: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and zolpidem due to the risk for additive CNS depression and next-day psychomotor impairment; dose adjustments may be necessary. Limit the dose of Intermezzo sublingual tablets to 1.75 mg/day.

## **Adverse Reaction**

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### **asthenia, drowsiness, fatigue**

Similar to other low-sedating antihistamines, somnolence/drowsiness (5% to 6%) and fatigue (1% to 4%) were reported with levocetirizine in clinical trials of adults and pediatric patients 12 years and older and at incidences greater than with placebo;

somnolence/drowsiness (3%) was also reported in clinical trials involving children aged 6 to 12 years. The combined incidence of drowsiness, fatigue, and asthenia was 8.1% for levocetirizine versus 3.1% for placebo in clinical study. Discontinuation due to somnolence/drowsiness, fatigue, or asthenia occurred in 2.3% of patients vs. less than 1% in placebo during long-term clinical trials. Adverse reaction profiles are similar regardless of the indication being treated.

### **cough, epistaxis, fever, infection, pharyngitis, xerostomia**

Side effects reported in 2% or more of levocetirizine-treated adult and pediatric patients 12 years of age and older, and at a greater incidence than seen with placebo, included: nasopharyngitis (4% to 6%), xerostomia (2% to 3%), and pharyngitis (1% to 2%). Cough (3%) and epistaxis (2%) have been reported in children 6 to 12 years of age receiving levocetirizine and at a greater incidence than with placebo. In children 1 to 12 years of age, pyrexia (fever) occurred in 4% of levocetirizine recipients. More pediatric patients 1 to 5 years of age receiving levocetirizine reported otitis media infection (3%) than with placebo (0%).

### **edema, hypotension, palpitations, sinus tachycardia, syncope**

Cardiovascular adverse events have been reported during levocetirizine therapy. In placebo controlled trials of levocetirizine in patients aged 12 years and older, more patients experienced syncope (0.2%) with levocetirizine than with placebo. World-wide postmarketing experience includes reports of palpitations, sinus tachycardia, and edema among levocetirizine treated patients. Severe hypotension has been reported in the postmarketing experience with cetirizine; levocetirizine is the active enantiomer of cetirizine.

### **appetite stimulation, weight gain**

Appetite stimulation has been reported during postmarketing experience with levocetirizine. In placebo controlled trials of levocetirizine involving patients aged 12 years and older, more patients experienced weight gain (0.5%) with levocetirizine than with placebo.

### **cholestasis, constipation, diarrhea, dysgeusia, elevated hepatic enzymes, hepatitis, nausea, vomiting**

Levocetirizine has been reported to cause transient elevations in bilirubin and liver function tests (elevated hepatic enzymes) at an incidence of less than 1%. These elevations were transient in all patients and did not require drug discontinuation. Vomiting and diarrhea have been reported in children aged 1 to 5 years during clinical

trials (4% vs. 3% placebo, incidence for both). In infants 6 to 11 months of age, diarrhea (13% vs. 4% placebo) and constipation (7% vs. 4% placebo) were reported and were the most common adverse effects in this population. Postmarketing experience includes reports of dysgeusia, nausea, cholestasis, and hepatitis; causal relationships have not been determined.

**agitation, depression, dizziness, dyskinesia, dystonic reaction, hallucinations, insomnia, myoclonia, paresthesias, seizures, suicidal ideation, tics, tremor**

Neurologic and psychiatric adverse events have been reported during levocetirizine therapy. In a study of the safety of levocetirizine in children 12 to 24 months of age, the following adverse events occurred more frequently with levocetirizine compared to placebo: agitation (0.4%), seizures (0.4%), febrile seizures (2%), insomnia (1.2%), and nervousness (0.4%). Dizziness, aggression, agitation, depression, febrile seizure, hallucinations, paresthesias, movement disorders (including dystonic reaction, oculogyric crisis), seizures (in those with a known seizure disorder), and tremor have been reported in world-wide postmarketing experience with use of levocetirizine in adults and children. Extrapyramidal symptoms, orofacial dyskinesia, myoclonia, tics, and suicidal ideation have been reported during postmarketing experience with cetirizine; levocetirizine is the active enantiomer of cetirizine.

**acute generalized exanthematous pustulosis (AGEP), anaphylactoid reactions, angioedema, dyspnea, pruritus, rash, urticaria**

Severe itching, or pruritus, has been reported in individuals discontinuing levocetirizine after long-term use. Individuals did not experience pruritus before initiating levocetirizine, but typically within a few days of stopping levocetirizine after daily use for a few months to years. Most individuals who experienced pruritus after discontinuation reported using levocetirizine for more than 3 months; however, some experienced this reaction after less than 1 month of use. Reported cases were rare but sometimes serious, with individuals experiencing widespread, severe itching that required medical intervention. The FDA identified 209 cases worldwide (197 domestic) of pruritus after discontinuation of levocetirizine ( $n = 27$ ), cetirizine ( $n = 180$ ), or both ( $n = 2$ ) supporting a causal relationship between stopping levocetirizine or cetirizine and pruritus. The number of pruritus cases increased with duration of use, suggesting that longer use may increase the risk for this reaction. Effective treatments have not been evaluated; however, symptoms resolved in most individuals who restarted levocetirizine or who tapered off after restarting. Instruct individuals on the risk of pruritus after discontinuing levocetirizine, especially if planned for chronic use. Anaphylaxis and hypersensitivity reactions have been noted during postmarketing experience with levocetirizine and/or

cetirizine (parent drug), including the following rare but potentially serious allergic or dermatologic events: anaphylactoid reactions, angioneurotic edema (angioedema), dyspnea, acute generalized exanthematous pustulosis (AGEP), fixed drug eruption, pruritus, rash, and urticaria. If signs or symptoms of hypersensitivity occur, discontinue levocetirizine.

### **hemolytic anemia, thrombocytopenia**

Levocetirizine is the active enantiomer of cetirizine; postmarketing reports of serious adverse reactions with cetirizine have included hemolytic anemia and thrombocytopenia.

### **dysuria, glomerulonephritis, urinary retention**

In postmarketing experience, dysuria and urinary retention have been reported with levocetirizine use, and glomerulonephritis has been reported with cetirizine use; causal relationships have not been established. Discontinue use if urinary retention occurs.

### **blurred vision, vertigo, visual impairment**

Unspecified visual impairment/disturbance and blurred vision have been reported with postmarketing use of levocetirizine. Vertigo has been reported as an ear or labyrinth disorder postmarketing. Causal relationships have not been established.

### **arthralgia, myalgia**

Musculoskeletal, connective tissues, and bone disorder adverse events reported with levocetirizine use postmarketing have included arthralgia and myalgia.

## **Description**

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Levocetirizine, the R-enantiomer of cetirizine, is a selective piperazine antihistamine (H1-blocker). Levocetirizine is effective in the treatment of seasonal allergic rhinitis, perennial allergic rhinitis, and chronic idiopathic urticaria. Levocetirizine has been used off-label for the symptomatic relief of atopic dermatitis. Despite reports of drowsiness with levocetirizine, controlled trials did not show it to cause adverse cognitive or psychomotor effects. Like its parent drug cetirizine, levocetirizine is considered "low-sedating", as it causes drowsiness to a lesser degree than first-generation (sedating) antihistamines. Rare but severe pruritus has been reported in individuals stopping levocetirizine after long-term use (daily use, typically for at least a few months and often for years) that may require medical intervention. Levocetirizine was initially FDA-

approved in 2007 as a prescription drug and was subsequently approved for nonprescription use in 2017.

## Mechanism Of Action

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Levocetirizine, the R-enantiomer of cetirizine, is highly selective for histamine H1-receptors. In vitro studies have demonstrated that levocetirizine has a 2-fold higher affinity for the H1-receptors than cetirizine. Levocetirizine, similar to other H1-antagonists, does not block the release of histamine, as do cromolyn and nedocromil, but rather competes with free histamine for binding at H1-receptor sites. This competitive antagonism blocks the effects of histamine on H1-receptors in the GI tract, uterus, large blood vessels, and bronchial smooth muscle. Levocetirizine suppresses histamine-induced skin reactions and associated pruritus. Blockade of H1-receptors reduces the edema, flare, and pruritus that result from histaminic activity. Levocetirizine, similar to the parent drug cetirizine, has a lower incidence of sedation compared to older antihistamines.

The inflammatory response plays a prominent role in the development of nasal obstruction in patients with allergic rhinitis and involves a number of mediators. Initial release of histamine from mast cells is followed by late-phase reactions involving a number of other cells, such as fibroblasts, epithelial cells, neutrophils, eosinophils (especially in conditions with raised IgE levels), macrophages, platelets, and lymphocytes. Cell adhesion can also be part of the inflammatory process. Levocetirizine has demonstrated anti-inflammatory effects in both in vitro and in vivo studies. The anti-inflammatory action appears to be related to a reduction in eosinophils, neutrophils, interleukin-4 and interleukin-8.

## Pharmacokinetics

Levocetirizine is administered orally. It is 91% to 92% protein bound. The mean volume of distribution is approximately 0.4 L/kg in both pediatric and adult patients. Only 14% undergoes metabolism via aromatic oxidation, N-dealkylation, O-dealkylation, and taurine conjugation; the remaining 86% is excreted unchanged. The elimination half-life in healthy volunteers was approximately 8 to 9 hours and is somewhat shorter in pediatric patients. Urinary excretion accounts for 85.4% of a dose and the feces for 12.9%. Renal clearance correlates with creatinine clearance; levocetirizine is excreted by both glomerular filtration and active tubular secretion.

Affected cytochrome P450 isoenzymes and drug transporters: CYP3A4  
CYP3A4 contributes to the metabolism of levocetirizine; however, clinically significant

drug interactions are not expected. Only 14% of levocetirizine is metabolized via aromatic oxidation, N-dealkylation, O-dealkylation, and taurine conjugation. The CYP3A4 isoenzyme is responsible for dealkylation; the enzymes responsible for aromatic oxidation have not fully been elucidated. In vitro studies have demonstrated that levocetirizine does not inhibit CYP1A2, 2C9, 2C19, 2A1, 2D6, 2E1, or 3A4. In addition, levocetirizine does not induce CYP1A2, 2C9, or 3A4. Formal drug interaction studies with levocetirizine have not been performed; data have been extrapolated from cetirizine studies.

## **Route-Specific Pharmacokinetics**

- Oral Route**

The oral tablet and oral solution are bioequivalent. Levocetirizine is rapidly absorbed from the GI tract with peak plasma concentrations reached in approximately 0.5 to 0.9 hours after administration. Steady state plasma concentrations are achieved in 2 days. Although the rate of absorption of the tablets may be increased and peak plasma concentrations reduced by 36% when administered with food, levocetirizine may be administered with or without food.

- Hepatic Impairment**

The effects of hepatic impairment on levocetirizine have not been studied. Approximately 72% of levocetirizine is renally cleared leaving only 28% for non-renal clearance; hepatic impairment is unlikely to result in significant change in levocetirizine clearance.

- Renal Impairment**

In patients with mild, moderate, and severe renal impairment, the AUC increased by 1.8-, 3.2-, and 4.3-fold, respectively, and the half-life increased by 1.4-, 2-, and 2.9-fold. In patients with renal failure (CrCl less than 10 mL/minute), the AUC and half-life increased by 5.7- and 4-fold, respectively. Dialysis removes less than 10% of levocetirizine from the blood. Dosing adjustment is necessary in patients with mild, moderate, or severe renal impairment. Levocetirizine should not be administered to adult patients with renal failure (CrCl less than 10 mL/minute), those on dialysis, or pediatric patients less than 12 years with renal disease, renal impairment, or renal failure.

- Pediatrics**

Children 6 years and older

In a single-dose pharmacokinetic study, 14 children (6 to 11 years of age) with mild allergic rhinitis received levocetirizine 5 mg PO. The following mean pharmacokinetic parameters were calculated: Tmax = 1.2 +/- 0.2 hours, Vd: 0.4 +/- 0.02 L/kg, Clearance: 0.82 +/- 0.05 mL/kg/minute (30% greater weight-normalized apparent body clearance than that of adults), and T1/2: 5.7 +/- 0.2 hours (24% reduction when compared to adults). The Cmax and AUC values were about 2-fold greater than those of healthy adult

subjects who also received a 5 mg dose in a cross-study comparison.

#### Infants and Children less than 6 years

In a pharmacokinetic study, 15 children (12 to 24 months of age) suffering from recurrent cough and other allergy-related symptoms received levocetirizine 0.125 mg/kg/dose PO twice daily for 90 days. The following mean pharmacokinetic parameters were calculated: Tmax: 1 hour, Vd: 0.37 L/kg, and T1/2: 4 hours. Pharmacokinetic parameters of children less than 6 years were calculated from a retrospective population pharmacokinetic analysis that included 324 subjects (181 children aged 1 to 5 years, 19 children 6 to 11 years, and 124 adults 18 to 55 years). Single or multiple oral doses ranging from 1.25 to 30 mg levocetirizine were administered; the data indicate that children aged 6 months to 5 years who receive 1.25 mg/day have drug plasma concentrations similar to those of adults who receive 5 mg/day.

- **Geriatic**

Data on levocetirizine pharmacokinetics in elderly patients are limited. Following daily administration of levocetirizine 30 mg for 6 days, the apparent total body clearance was 33% lower in 9 elderly patients aged 65 to 74 years compared to younger adults. Additional pharmacokinetic data in elderly patients are not available. Since cetirizine clearance is correlated to renal function and not age, it is believed that the same is true for levocetirizine.

## Administration

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

### Oral Administration

Administer once daily in the evening.

May administer with or without food.

### Oral Solid Formulations

Tablets

If tablet is scored it may be split in half if a lower dosage is needed.

### Oral Liquid Formulations

Oral solution

Administer using a calibrated measuring device to ensure accurate dosing.

## Maximum Dosage Limits

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- **Adults**  
5 mg/day PO.
- **Geriatric**  
5 mg/day PO.
- **Adolescents**  
5 mg/day PO.
- **Children**  
12 years: 5 mg/day PO.  
6 to 11 years: 2.5 mg/day PO.  
3 to 5 years: 1.25 mg/day PO.  
1 to 2 years: 1.25 mg/day PO; up to 0.125 mg/kg/dose PO twice daily has been used off-label for atopic dermatitis.
- **Infants**  
6 to 11 months: 1.25 mg/day PO.  
Less than 6 months: Safety and efficacy have not been established.

## Dosage Forms

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- CVS Allergy Relief 24 Hour 5mg Tablet
- Equate Allergy Relief 24 Hour 5mg Tablet
- GNP Allergy Relief 24 Hour 5mg Tablet
- GNP Allergy Relief 24 Hour 5mg Tablet
- Leader 24HR Allergy Relief 5mg Tablet
- Levocetirizine 2.5mg/5mL Oral solution
- Levocetirizine 5mg Oral tablet
- Levocetirizine Bulk powder
- Nazirex Compounding Kit
- Quality Choice Levocetirizine 5mg Tablet
- Walgreens Allergy Relief 24 Hour 5mg Tablet
- Walgreens Levocetirizine 5mg Tablet
- Xyzal Allergy 24 Hour 5mg Tablet
- Xyzal Allergy 24 Hour 5mg Tablet
- Xyzal Children's Allergy 24 Hour 2.5mg/5mL Solution (Tutti Frutti)

## Dosage Adjustment Guidelines

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### Hepatic Impairment

No dosage adjustment is needed.

## **Renal Impairment**

For adults, adolescents and children 12 years and older, the following dosage adjustments for renal impairment are recommended :

CrCl 50 to 80 mL/minute: 2.5 mg PO once daily.

CrCl 30 to 50 mL/minute: 2.5 mg PO once every other day.

CrCl 10 to 30 mL/minute: 2.5 mg PO twice a week; administered every 3 to 4 days.

CrCl less than 10 mL/minute: Contraindicated.

Infants and Children 1 to 11 years: According to the FDA-approved prescription label, the use of levocetirizine in pediatric patients less than 12 years of age with any degree of renal impairment is contraindicated.

### **Intermittent hemodialysis**

Use of levocetirizine in patients undergoing hemodialysis is contraindicated.

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