mind

For better
mental health

Making sense of antidepressants

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Making sense of antidepressants

The different types of antidepressant

This booklet is aimed at anyone interested in learning more about antidepressants. It starts with general information that applies to all antidepressants, then gives information specific to the different types of antidepressant, followed by details specific to the individual drugs. It's therefore important to read the general as well as the specific information in order to get all the information about the drug you are taking.

What should I know before taking any drugs?

Drug names

Drugs can have two types of names: their general (generic) name and the trade names given by the drug companies (starting with a capital letter). The same drug can have several different trade names. In this booklet, drugs are listed using their generic name, with the trade name/s after it in brackets.

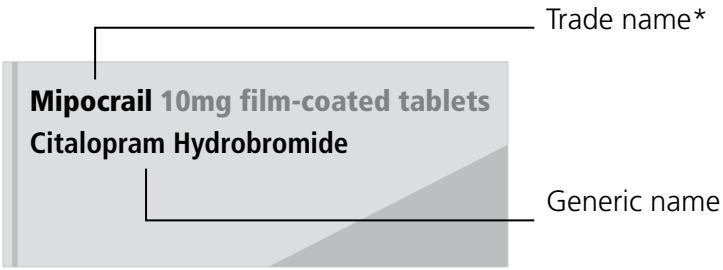

Figure 1. Typical name display on packaging

**This is just an example, there isn't really a brand of citalopram called Mipocrail.*

Informed consent
Though there are exceptions (see *Mind rights guide 3: consent to medical treatment*), generally, you can only receive treatment that you have specifically agreed to. The law says that you have the right to make an informed decision about which treatment to have, and whether or not to accept the treatment a doctor suggests. To consent properly, you need to have enough information to understand the nature, intended benefits and possible harms of the treatment, including its chance of success, and available alternative treatments

Even after you have given your consent you can change your mind at any time. Consent is fundamental to treatment, and treatment given without consent can amount to assault and negligence.

Patient information leaflets
If you are prescribed medication as an outpatient, or by your GP, it should come with a patient information leaflet (PIL) in accordance with a European Union directive. As an inpatient, you may have to ask for it specifically. If you do not receive this information with your medicine, or accidentally throw the PIL away (it's usually folded up small to fit in the packet with the tablets), you should ask for it from the person who makes up your prescription.

The PIL contains information such as:
- the trade and general (generic) names of the drug
- the strength of the medicine and the form it takes – for example, tablets or a liquid
- who should take it
- what conditions the drug is licensed to treat
- any cautions you should be aware of before taking it, such as conditions which mean you should take a reduced dose or not take it at all
- how to take it
- when to take it

- possible side effects
- the expiry date
- how to store them safely.

It should also contain a full list of all the ingredients, including the extra contents that hold it together as a tablet or capsule, such as maize starch, gelatin, cellulose, and colourings. This information is important because some people may be allergic to one or other of the ingredients, such as lactose or gluten or a colouring. Gelatin is unacceptable to some people because it is an animal product.

The final item on the leaflet tells you that it contains only the most important information you need to know about the medicine, and that if you need to know more, you should ask your doctor or your pharmacist.

Some of the information is quite hard to understand, and the Commission on Human Medicines, an advisory body of the Medicines and Healthcare products Regulatory Agency (MHRA), has been looking at ways of making it easier. They have produced information and advice for consumers which is available on the MHRA website in the Safety Information section. There is more information on medicines and their use, in the form of Medicines Guides, available from the EMC (Electronic Medicines Compendium) website. (See *Useful websites* on p.52 for details of both these organisations.)

Getting more information from your doctor or pharmacist

Many people would like to have the information about their proposed treatment before they are given the prescription for it, and not after they have got it from the pharmacist and taken it home. The following are issues you might like to discuss with your doctor when she or he gives you a prescription for a drug:

- What is the name of the drug, and what is it for?
- How often do I have to take it?

- How long will I have to take it for?
- If I am taking any other drugs, will it be all right to take them together? – Though there are systems in place to help prescribing doctors and pharmacists identify drug conflicts, it can be helpful to clarify them yourself.
- Will I still be able to drive?
- What are the most likely side effects, and what should I do if I get them?
- Do I have to take it at any particular time of day?
- Is it likely to make me sleepy?
- Should I take it with food?
- When I want to stop taking it, am I likely to have any problems with withdrawal?

You may well think of other questions you wish to ask. You should also consider talking to your pharmacist. Pharmacists are drug specialists, and may be more knowledgeable about your drugs than the doctor who prescribes them. They may be more aware of possible side effects, and also possible interactions with other drugs (these occur when one drug changes the effect of other drugs you are taking; making them less effective, or causing additional side effects). Pharmacists are usually very willing to discuss drugs with patients, and most pharmacists have space set aside where you can talk privately.

Since January 2006, a scheme has been in place called the 'Medicines Use Review'. If you regularly take more than one prescription medicine, or take medicines for a long-term illness, you are encouraged to go to pharmacists who are operating the scheme, for a full discussion of your medicines, what they're all for, and any problems you may have with them. A guide to the scheme is available on the Department of Health website. (See *Useful websites* on p.52.)

What are antidepressants for?

Antidepressants are primarily used to treat depression. Many are also licensed for other conditions such as various forms of anxiety.

Some tricyclic antidepressants (see p.20) are licensed for phobias and obsessional states; some of the SSRIs (see p.32) and SNRIs (see p.39) are licensed for panic disorder, generalised anxiety, obsessive compulsive disorder, social anxiety disorder, bulimia nervosa (an eating disorder), post-traumatic stress disorder; moclobemide (see p.31) is licensed for social anxiety.

Antidepressants are not the only form of treatment for any of these conditions. More detailed information on each of these diagnoses, as well as alternative treatment options, is available from Mind (see *Useful organisations* on p.51.)

Some of the tricyclics (see p.20) are used to treat different types of pain in adults, and bed-wetting in children.

How do antidepressants work?

Neurons (nerve cells) communicate with one another via brain chemicals called neurotransmitters, which are released by one neuron and interact with receptors on another neuron. Their action is usually terminated by being taken back up into the neuron that released them (re-uptake).

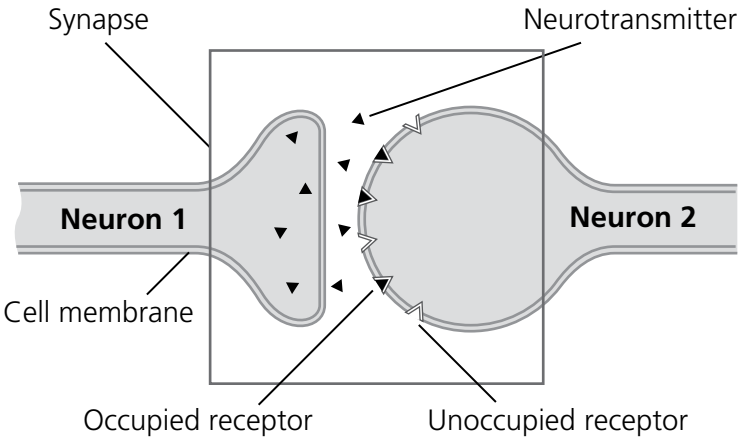

Figure 2. Neurons & neurotransmitters
Neurons travelling between neurotransmitters
From *The science of the mind: investigating mental health Science: Level 2 Book 1 Core Concepts in Mental Health (Open University, 2010). Reproduced with permission.*

Depression is thought to be associated with low levels of certain neurotransmitters, particularly noradrenaline (also known as norepinephrine) and serotonin (also called 5-hydroxytryptamine or 5-HT). Most antidepressant drugs are therefore designed either to prolong the effects of the neurotransmitters by blocking their re-uptake into the neuron that released them, or to increase the amount that is accumulated in that neuron and so available for release. Most types of neurotransmitters work at several different sites in the brain, and in other parts of the body as well. This means that drugs that interfere with neurotransmitters in the brain will affect the same neurotransmitters in other parts of the body and brain causing 'side' effects, that is, not the intended effect of the drug. As researchers find out more about the specific actions of

different neurotransmitters, they classify their receptors into different subtypes, depending on what response they cause. In designing new antidepressants, the aim is usually to target the drug only on brain receptors thought to be directly involved with depression, and to avoid changing the action of the neurotransmitter at other sites.

How effective are antidepressants?

Psychiatric research indicates that:

- Antidepressants can be effective for some people. However, recent analysis of research studies has suggested that they may be no more effective than a placebo (a dummy drug) for many people. Their use has been influenced by the fact that the advantage of antidepressants over placebo may be exaggerated by the research methods used, and positive research results are much more likely to be published than negative results.
- In milder depression, short-term psychotherapy or counselling is as effective as drugs (see *Understanding talking treatments*, Mind, 2009) in alleviating symptoms.
- A high proportion of people with depression recover spontaneously without treatment.
- The use of antidepressants has not affected rates of depression or suicide. If your depression is related to housing, financial or other social problems, practical resolutions to these difficulties might be the most appropriate way of shifting your depression.

Many people find that they are best helped with a combination of an antidepressant and a talking therapy or social help.

If you have severe depression and one antidepressant is not effective, your doctor may suggest that you take an additional drug. This must be done with great care, because some drugs are dangerous in combination, but research suggests, for example, an SSRI combined with mirtazapine may be more effective than the SSRI alone in severe depression (see p.39 for details of individual drugs).

How long do they take to start working?

No-one knows why, but people report that most antidepressants take two to four weeks to take effect, although this may not be the case for some of the newest drugs.

Some doctors have attempted to speed up the response to antidepressants by combining them with pindolol (a beta blocker). So far, the results of these trials have been mixed. For some people, the combination produced a faster and more effective response; for others pindolol made no difference. If you have severe depression and antidepressants have proven unsuccessful in treating your symptoms, you could consider this before considering other drugs, such as lithium, or other therapies, such as electroconvulsive therapy. The most common adverse effects of pindolol are low blood pressure, headache, nausea, diarrhoea and increased irritability.

What sorts of side effects can occur?

Some people who are prescribed antidepressants stop taking them because of unpleasant and worrying side effects.

If you are already depressed, struggling with some of the drugs' adverse effects may make you feel even more distressed, especially as the worst of these effects tend to occur at the beginning of treatment, before the drugs have started to lift the depression.

'*With most antidepressants I get initial, horrid side effects that wear off within 4 weeks, typical ones being lethargy, drowsiness and nausea. Hang in there for 4 weeks and they will more than likely pass.*' Nicky Palmer, Mindlink member

You may not experience any of the adverse effects listed in this booklet, or the ones that affect you may be no more than a minor inconvenience, which you consider an acceptable price to pay for the benefits the drugs give you. You are the best judge as to whether or not the drugs are working for you. However, if they do cause troublesome or unpleasant side effects, don't hesitate to tell your doctor.

The National Institute for Health and Clinical Excellence (NICE) suggests that, when prescribing antidepressants, doctors should see you every 2–4 weeks in the first 3 months and at longer intervals thereafter, if response is good. If you are at risk of harming yourself, doctors should keep in close contact with you, especially at the beginning of your treatment. You should be able to visit your doctor to discuss any adverse effects you experience. You can also report your side effects to the MHRA using the Yellow Card Scheme (see *Useful organisations* on p.51.)

The frequency of possible side effects listed in PILs is defined using the following system:

Very common - Affects more than 1 person in 10

Common - Affects 1 to 10 people in 100

Uncommon - Affects 1 to 10 people in 1,000

Rare - Affects 1 to 10 people in 10,000

Very rare - Affects less than 1 person in 10,000

Not known - Frequency cannot be estimated from the available data

These categories are used below, under the individual drugs, when this information is available.

Side effects which may happen with all antidepressants

SIADH (Syndrome of Inappropriate Antidiuretic Hormone Secretion)

There is a warning from the Commission on Human Medicines about low blood sodium levels (hyponatraemia) with some antidepressants. Antidiuretic hormone (vasopressin) is one of the hormones that controls the production of urine. If too much is secreted, the body holds on to water and becomes low in sodium. This mainly affects older people and may cause memory problems, difficulty concentrating, drowsiness and falls. If sodium levels are very low, it may lead to confusion, hallucinations, fits, loss of consciousness and death. SIADH is a rare side effect, mainly of tricyclic and antidepressants, SSRIs and SNRIs.

Tooth decay

Saliva is important in protecting against tooth decay, and drugs that cause a dry mouth may cause tooth decay as a secondary effect. There have been several reports of people developing dental problems when using these drugs, especially after long-term use of tricyclic and related antidepressants.

Suicidal feelings

There is a possibility that taking antidepressants may make people feel suicidal when they had not felt this way before they started the medication. Suicidal feelings have mainly be associated with SSRI antidepressants, with many published anecdotes, but there is a suggestion that the same thing may occur with all types of antidepressants. It is possible that when someone is very depressed they cannot summon up the motivation or energy for suicide, and in the early stages of treatment this changes, so that they then do have the energy to act, before the depression has really started to lift. This has usually been the explanation for suicide in the early stages of treatment. However, the suggestion that the drugs themselves cause suicidal thoughts and urges is increasingly being taken seriously, and this issue is discussed later (see p.33) in relation to SSRI antidepressants in particular. However, research suggests that all antidepressants carry similar risks.

The BNF (*British National Formulary,* which is the main reference book used by doctors, listing all available medicines) contains the following warning: 'The use of antidepressants has been linked with suicidal thoughts and behaviour. Where necessary patients should be monitored for suicidal behaviour, self-harm, or hostility, particularly at the beginning of treatment or if the dose is changed.'

If someone is so depressed that they sometimes feel suicidal, it might be advisable for a relative or close friend to help them to look after their tablets so the right dose is taken at the right time.

Diabetes

Long-term (several years) use of antidepressants is associated with an increased risk of diabetes, especially in people over the age of 30, taking SSRIs or tricyclics.

Serotonin syndrome

This is serious and potentially fatal. The symptoms are (most common first):

- headache
- feeling sick
- diarrhoea
- high temperature, shivering, sweating
- high blood pressure, fast heart rate
- tremor, muscle twitching, over-responsive reflexes
- convulsions (fits)
- agitation, confusion, hallucinations
- loss of consciousness (coma).

It may occur with any antidepressant, but is more likely with SSRIs, especially if they are given with other antidepressants including MAOIs, tryptophan and lithium. It may come on very suddenly.

Neuroleptic malignant syndrome

The BNF warns that this very serious condition, which is more often associated with antipsychotic drugs, may occur, rarely, with antidepressants. The symptoms include high temperature, changes in the level of consciousness, stiffness, pale skin, fast heart rate, unstable blood pressure, sweating, and urinary incontinence.

Antidepressants may affect driving and other skilled tasks.

How long should I stay on antidepressants?

Studies show that you may be less likely to become depressed again if you stay on your antidepressants for at least six months. The BNF recommends that people should keep taking the effective dose for at least six months (about 12 months in older people) after the depression has lifted. If you stop treatment too soon, the depression is likely to come back. If you have recurrent depression, you may need to take an effective dose of your antidepressants for several years. (Information about maintenance doses is included under the individual drugs.) Some studies suggest that most people aren't being given sufficient antidepressants for long enough.

Because of possible problems with withdrawal (see the next section), it is important not to suddenly reduce the dose or stop altogether. If possible you should discuss with your doctor or another professional how long to remain on your antidepressants and how to go about stopping them.

What happens when I stop taking them?

Withdrawal reactions can occur with all major types of antidepressants. Problems are more likely to occur if you stop taking them suddenly or if you have been taking them for a long time. Withdrawal symptoms usually start suddenly within a few days of stopping the antidepressant, or of reducing its dose. Individuals vary as to whether they get withdrawal problems: some people may stop taking their drugs with no problems, while others experience extremely unpleasant withdrawal symptoms and have to reduce the dose very slowly over a long period. The difficulties are also related to the 'half-life' of the drug: this is an estimate of how long it takes for a drug to be eliminated from the body. The drugs with the shortest half-lives cause the greatest problems with withdrawal (see *Useful websites* on p.52 for more information).

Withdrawal problems vary, depending on the type of antidepressant. Common symptoms include gastric problems (nausea, vomiting, abdominal pain or diarrhoea), loss of appetite, sleep disturbance (insomnia, vivid dreams or nightmares), general discomfort (sweating, lethargy or headaches), and mood changes (low mood, hypomania – 'high' moods, panic, anxiety or irritability) and extreme restlessness. With SSRIs, the commonest symptoms appear to be dizziness, light-headedness, numbness, tingling and sensations that feel like electric shocks. When withdrawal symptoms are severe, they may prevent people from going out and leading a normal life, and are particularly dangerous with activities like driving.

The BNF recommends that if antidepressants have been prescribed continuously for eight weeks or more, they should not be stopped abruptly, but should be reduced gradually over four weeks. For many people four weeks will not be long enough and withdrawal will have to be more gradual over a much longer period.

A list of possible withdrawal symptoms that you may experience can be found under the relevant group of antidepressants or the individual drug, if appropriate. This information may help you to distinguish a brief and temporary withdrawal period from what may otherwise be mistaken for a re-emergence of the earlier depression or distress. For more information on withdrawal, see Mind's booklet, *Making sense of coming off psychiatric drugs*.

Are antidepressants addictive?

Drug companies and some doctors have often said that antidepressants are not addictive, because if drugs are addictive, people develop a craving for them if they stop taking them suddenly, find the need to increase the dose to maintain the same effect, and use the drug to get high. They have alleged that none of these things happens with antidepressants. However, after taking them for some time, some people do become 'tolerant' to antidepressants and report needing to take higher doses to achieve the same effect. People also may consider that they are 'addicted' if they find that they experience withdrawal symptoms when they stop taking them, and have to go back on them and cut down slowly.

Although antidepressants don't usually produce the sort of 'buzz' that results in cravings, some of them are used as street drugs, indicating that they do have the potential to have this effect. For example, people can get slightly high from the stimulant effect of the monoamine oxidase inhibitor (MAOI) antidepressant tranylcypromine.

If you have been taking antidepressants for a long time, you may also develop a psychological dependency on them, and worry that you may not be able to cope without them. You may find it helpful to join a group of other people who are withdrawing from medication, or have successfully done so.

When shouldn't I take antidepressants?

Pregnant and nursing mothers

Because a few drugs have been proved to cause birth defects, and drugs are not tested in pregnant women, you should be very cautious about taking drugs during pregnancy. You need to balance the needs of the mother-to-be against the possible risk to the unborn child, particularly in the first three months of pregnancy and in the last few weeks before the birth.

NICE recommends stopping SSRIs, and paroxetine in particular, when pregnancy is confirmed, or preferably before conception, and if drugs are essential, using tricyclics which are considered to be less risky in the early months of pregnancy.

Research suggests that taking antidepressants in pregnancy increases the risk of miscarriage and of congenital problems as well as premature birth. There is evidence that taking SSRIs early in pregnancy slightly increases the risk of heart defects, spina bifida, and cleft palate and hare lip.

Tricyclic antidepressants, SSRIs and SNRIs given in late pregnancy have been associated with withdrawal symptoms in newborn babies. Tricyclics are associated with rapid heartbeat, irritability, muscle spasms, restlessness, sleeplessness, fever and fits. SSRIs and SNRIs have been associated with jitteriness, poor muscle tone, weak cry, respiratory distress, low blood sugar and fits, and high blood pressure in the lungs in the newborn infant.

After the birth, a nursing mother is likely to pass any drugs she is taking to her baby through her breast milk. Newer drugs carry a higher risk than drugs that have been in use longer, simply because less is known about them. Doxepin (Sinepin), in particular, should be avoided in breastfeeding.

Some drugs present much less of a risk and its worth discussing the choice with your prescriber if you wish to breastfeed.

When a woman who is pregnant or who is breastfeeding is suffering from depression, every effort should be made to find non-drug treatments. With help and support, drugs may be unnecessary. (Also see Mind's booklet *Understanding postnatal depression*.)

Children and antidepressants
Antidepressant drugs are not licensed for the treatment of depression in children under 16. The NICE guideline on depression in children and young people, published in September 2005, recommends that antidepressants should only be given to children in combination with psychological therapies, unless the child has refused these.

The only antidepressant that should be used initially is fluoxetine (Prozac), because this is the only one whose benefits outweigh its possible harms in children, and this is the only antidepressant listed in the *BNF for Children*. Fluoxetine should be prescribed by a child psychiatrist. If fluoxetine cannot be used, citalopram or sertraline may be tried. Paroxetine, venlafaxine, St John's wort and tricyclic antidepressants should not be used. Antidepressants are not tested in children and when used they should be started cautiously at a dose appropriate to the child's size.

Because of reported cases of suicidal thoughts, suicide, self-harm and violence – especially by young people taking these drugs – children should be carefully monitored, especially at the start of treatment or if the dose is being changed (either increased or reduced).

The following tricyclics are licensed for the treatment of bedwetting: amitriptyline, imipramine and nortriptyline.

If you are taking other drugs
If you are prescribed antidepressants, it's important to tell your doctor about any other drugs you are taking, including anything you have bought over the counter, as antidepressants can interact with a number of different types of drug, and some combinations can be dangerous. Where combinations of psychiatric drugs are known to interact, these have been listed further in this booklet. Sometimes, a number of interacting psychiatric drugs are prescribed together, which can add to the adverse effects of the individual drugs.

Alcohol

People taking antidepressants should be careful about drinking alcohol. Alcohol is a depressant and may be one of the things that's making you depressed in the first place: some people are made very depressed by particular alcoholic drinks, but may be unaware that this is the cause. Alcohol interacts with most antidepressants, increasing sedation and affecting the ability to perform skilled tasks even further. It can make older people more prone to falls and confusion. It's therefore wise to ask your doctor or pharmacist whether it's safe to drink alcohol with the drug you are taking.

All information about drug doses mentioned in this booklet is taken from recommendations in the *British National Formulary (BNF)* and drug data sheets available on the electronic *Medicines Compendium (*see *Useful websites* on p.52). It is very dangerous to take more than the prescribed dose; although, sometimes, doses higher than the stated maximum can be given in hospital under close supervision. The trade names of the drugs are in brackets after the generic name.

Tricyclic and related antidepressants

Tricyclics have been in use since the 1960s. They affect the transmitter systems of the two brain chemicals (neurotransmitters – see figure 2, p.7) noradrenaline and serotonin.

Related drugs (mianserin and trazodone, see p.26) have a similar chemical structure and action to the tricyclics, but have different adverse effects.

Tricyclic drugs also affect a third neurotransmitter (acetylcholine), causing side effects to the heart and blood circulation system. These are called 'anticholinergic' or 'antimuscarinic' effects: drowsiness, dry mouth, blurred vision, constipation, rapid heartbeat, difficulty passing water and sweating.

Some of these drugs are more sedating than others, and this may affect the choice of the most appropriate drug for an individual: if you are feeling agitated and having difficulty sleeping, a sedating antidepressant may be most helpful.

More sedating tricyclics	Less sedating tricyclics
amitriptyline, clomipramine, dosulepin, doxepin, mianserin, trazodone	imipramine, lofepramine, nortriptyline

Table 1. The sedative properties of different tricyclics

Cautions

This group may affect the ability to perform skilled tasks such as driving or operating machinery. These drugs can affect the heart and circulatory system and should not be given to people who have had a recent heart attack, or have heart block. They should not be given to people who have manic episodes or severe liver disease. Older people find the adverse effects of tricyclics a particular problem, as low blood pressure can lead to dizziness, fainting and falls; therefore, it is important to start on a low dose and increase gradually.

They should be used with caution in people with diabetes, heart, liver or thyroid disease, the eye disease glaucoma, and for anyone already experiencing problems passing water.

The BNF says, 'Tricyclic and related antidepressant drugs should be used with caution in patients with a significant risk of suicide, or a history of psychosis or bipolar disorder, because antidepressant therapy may aggravate these conditions'.

If you have epilepsy, this group of antidepressants can make you more likely to have fits, and you should not take them if you are receiving treatment with ECT or anaesthetics.

It is very dangerous to take more than the stated dose.

Interactions between tricyclics and other psychiatric drugs
A tricyclic taken with some antipsychotics, such as chlorpromazine (Largactil), can make the adverse effects much worse. If they are taken with minor tranquillisers or sleeping pills, such as diazepam (Valium), the sedative effect increases.

They should not be taken with MAOI antidepressants or for at least two weeks after stopping an MAOI (see p.28).

Tricyclics interact with SSRIs (see p.35 for more details).

Withdrawal from tricyclics
People withdrawing may experience the following more common symptoms:
- a flu-like illness, which can include nausea, vomiting, abdominal pain, loss of appetite, diarrhoea, generally feeling unwell, chills, weakness, tiredness, sweating, and headache
- jitteriness, anxiety, agitation and panicky feelings
- difficulty getting to sleep, followed by very vivid dreams early in the night, which can be frightening.

There are a few reports of people developing disturbed and extremely excitable (manic) behaviour. On rare occasions, if the drug is stopped abruptly, panic attacks may occur. (See, in particular, amitriptyline and imipramine below.)

Tricyclics

Amitriptyline hydrochloride (also in the compound Triptafen, combined with the antipsychotic, perphenazine)
The BNF says that, although this drug is effective, it should not be used to treat depression because it is dangerous if you take too much.

Form: tablets or liquid.
Dose: *Adults:* 50-75mg daily initially, in divided doses or as a single dose at bedtime; increased gradually as needed to a maximum dose of 150mg. *Older people and adolescents: 30-75mg. Children: may be* used to treat bedwetting for a maximum of three months.
Side effects (most common first): dry mouth, sedation, drowsiness, blurred vision, constipation, nausea, difficulty passing water. Heart and circulatory system effects: changes in heart rhythm, rapid heartbeat, low blood pressure on standing, fainting (particularly at high doses and in older people). Sweating, tremor, rashes and allergic reactions, disturbed behaviour (particularly in children), manic episodes, confusion (particularly in older people), reduced sexual arousal and interference with sexual function, blood sugar changes and weight changes (usually gain). Hormone-related effects: enlargement of testicles, breast development and secretion of milk. Fits, movement disorders, fever, blood disorders, low blood sodium levels, abnormal liver function.
Withdrawal: an estimated 80 per cent of people may experience withdrawal symptoms. Children may find these symptoms particularly distressing.

Clomipramine (Anafranil, Anafranil SR)

Clomipramine is also given for obsessional states, when the doses given may be higher than for depression.
Form: tablets or capsules. Anafranil SR is a modified release form.
Dose: *Adults:* 10mg daily initially, increasing gradually as necessary to 30-150mg maximum daily. Usual maintenance dose 30-50mg daily. *Older people:* 10mg daily initially, increased to 30-50mg daily.
Side effects:
Very common: nausea, dry mouth, sweating, constipation, problems focussing eyes and blurred vision, disturbances of urinating; drowsiness, transient fatigue, feelings of unrest, increased appetite; dizziness, tremor, headache, muscle spasms; weight gain, disturbances

of libido and potency.
Common: vomiting, abdominal disorders, diarrhoea, loss of appetite; hot flushes, dilated pupils; confusion with disorientation and hallucinations (particularly in older people and those with Parkinson's disease), anxiety, agitation, sleep disturbances, mania, hypomania, aggressiveness, poor memory, yawning, depersonalisation, sleeplessness, nightmares, aggravated depression, difficulty concentrating; delirium, speech disorders, pins and needles, muscle weakness, increased muscle tone; low blood pressure when standing up, fast heart rate, and changes in heart rhythm, palpitations; changes in liver function; allergic skin reactions (skin rash, itching), sensitivity to light; breast enlargement, milk secretion; taste disturbances, ringing in the ears.
Uncommon: increased psychotic symptoms; fits, unsteadiness; increased blood pressure.
Very rare: glaucoma; high temperature; liver disease with or without jaundice; fluid retention (local or generalised), hair loss; blood disorders; bleeding in the skin; lung inflammation, with or without blood disorder, anaphylactic reaction including low blood pressure; disturbance of regulation of urine production.
Drug interactions: see MAOIs on p.28.

Dosulepin (Prothiaden)

The BNF says that, although this drug is effective, it should not be used to treat depression because it is dangerous if you take too much. It should only be prescribed by specialists.
Form: tablets or capsules.
Dose: *Adults:* 75mg daily initially, increased as necessary up to a maximum 150mg daily. *Older people:* 50-75mg.
Side effects: see amitriptyline (p.22). Because there is a small margin of safety between the maximum therapeutic dose and a dangerous overdose, the Commission on Human Medicines advises that use of dosulepin in new patients should be avoided, it should be started only by specialists, and prescribers should limit the amount issued.

Doxepin (Sinepin)

Form: capsules.
Dose: *Adults:* 75mg daily initially, in three divided doses, increased as necessary up to a maximum of 300mg daily in three divided doses (up to 100mg at one dose). *Older people:* 10-50mg daily initially. 30-50mg daily may be enough.
Side effects: see amitriptyline (p.22).
Caution: avoid while breastfeeding.

Imipramine

Form: tablets.
Dose: *Adults:* 75mg daily initially, in divided doses, increased gradually as necessary up to a maximum 150-200mg (up to 300mg in hospital patients). Up to 150mg may be given as a single dose at bedtime. *Older people:* 10mg daily initially, increased gradually to 30-50mg daily. *Children:* may be given to children over six years old for bedwetting.
Side effects: see amitriptyline (p.22).
Withdrawal: studies show that 21 to 55 per cent of people experience gastric and other bodily discomforts.

Lofepramine (Feprapax, Lomont)

Form: tablets or liquid.
Dose: *Adults:* 140-210mg daily in divided doses. *Older people:* older people may respond to lower doses.
Side effects: like amitriptyline (p.22), but less sedating, and fewer side effects reported. Reports of liver disorders.
Caution: to be avoided in people with liver or severe kidney disorders.

Nortriptyline (Allegron)

Form: tablets.
Dose: *Adults:* low dose initially, increasing gradually as necessary up to 75-100mg daily in divided doses or as a single dose. (Blood to be monitored if dose is any higher.) Maximum dose 150mg in

hospital patients. *Older people and adolescents:* 30-50mg initially in divided doses. *Children:* may be used for bedwetting for a maximum of three months.
Side effects: see amitriptyline.

Trimipramine (Surmontil)
Form: tablets or capsules.
Dose: *Adults:* 50-75mg daily initially, as a single dose two hours before bedtime, or as 25mg at midday and 50mg in the evening, increasing as necessary up to a maximum dose of 300mg daily for four to six weeks. *Older people:* 10-25mg three times daily initially, half the adult maintenance dose may suffice.
Side effects: see amitriptyline.

Tricyclic-related antidepressants

Mianserin hydrochloride
Form: tablets.
Dose: *Adults:* 30-40mg daily initially, in divided doses or as a single dose at bedtime. Increased gradually as necessary. Usual dose range 30-90mg. *Older people:* 30mg daily initially.
Side effects: similar to amitriptyline, but said to be fewer and milder antimuscarinic effects and other effects on the heart and circulatory system. Other unwanted effects may include jaundice, arthritis, and pain in the joints.
Caution: in rare cases may cause serious blood disorders, especially in older people. Blood tests every four weeks recommended during the first three months of treatment. See your doctor if a fever, sore throat, sore mouth or other infection develops.

Trazodone hydrochloride (Molipaxin)
Form: tablets, capsules or liquid.
Dose: *Adults:* 150mg daily in divided doses after food or as a single dose at bedtime, increased as necessary up to 300mg daily.

Hospital patients up to a maximum of 600mg daily in divided doses. *Older people:* 100mg daily.
Side effects: similar to amitriptyline (p.22), but fewer antimuscarinic effects and other effects on the heart and circulatory system; may be more sedating. *Rarely:* priapism – persistent erection in men; if this occurs you should stop taking the drug and see a doctor immediately.

Monoamine oxidase inhibitors (MAOIs)

MAOIs work on the same neurotransmitters as the tricyclics (noradrenalin and serotonin), but act by blocking the enzymes that break them down. Blocking the enzymes enables the transmitters to accumulate so that more is released. Because of their side effects, fewer MAOIs tend to be prescribed and, usually, only when other antidepressants (tricyclics or SSRIs) have failed. The BNF recommends that they should only be prescribed by specialists. It may take three to five weeks for MAOIs to work.

Avoiding certain foods and drinks

MAOIs can cause a dangerous reaction to certain foods and drinks, so you should be very careful about what you consume (you should be given a treatment card with advice on what to avoid). Steer clear of anything that is not fresh, which has been fermented, pickled, cured, hung, dried or matured. This is because when food is exposed to the air, a substance called tyramine – which causes this dangerous interaction with MAOIs – rises to high levels. Excluded foods include:

- cheese
- game
- pickled fish
- dry sausage such as salami
- textured vegetable protein
- liver
- yoghurt
- overripe fruits
- yeast extracts such as Marmite, Bovril or Oxo
- alcohol (especially red wine)
- non-alcoholic beer and lager
- soya extract
- broad bean pods
- banana skins.

If you do eat or drink any of these, it may result in a dangerous rise in blood pressure and severe throbbing headache. You should contact your doctor immediately if this happens or you are concerned about something you have eaten. Fortunately, serious incidents and deaths are rare.

When MAOIs are not suitable

MAOIs should usually be avoided by people who tend to get agitated, or who have liver, kidney or heart disease, epilepsy, diabetes, and blood disorders. They should not be given to children, and only with great caution, if at all, to older people. Tranylcypromine is the most hazardous, because of its stimulant effect.

Drug interactions with MAOIs

It may be dangerous to take MAOIs at the same time as certain other prescribed or over-the-counter medicines, whether these are tablets, capsules, nose drops, inhalations or suppositories. Cough mixtures and cold treatments should be avoided. Always check with your GP first, and always tell your dentist about the medication you are taking before treatment. Do not use with the following psychiatric drugs:

- Tricyclic and other antidepressants. It is essential to have a gap after stopping these, before starting MAOIs. Leave at least one week after stopping SSRIs; five weeks after fluoxetine (Prozac); two weeks after paroxetine (Seroxat) and sertraline (Lustral). Always wait at least 14 days after finishing a course of MAOIs before starting a different antidepressant. It is particularly dangerous to combine clomipramine (Anafranil) and tranylcypromine.
- Carbamazepine (Tegretol) given for manic depression or epilepsy.
- Certain antipsychotic drugs (neuroleptics) prescribed for severe mental distress such as hallucinations and delusions, because their effects may be heightened.

Withdrawing from MAOIs
This is a similar experience to coming off tricyclics (see p.22). It is important to reduce the dose gradually. Continue with food and drink restrictions for two weeks after stopping completely. Avoid abrupt withdrawal, unless there's good reason, because fits may occur. There have been rare reports of abrupt withdrawal resulting in hallucinations or delusions. People may have difficulty coming off tranylcypromine because of its stimulant effect.

A few people take larger doses than prescribed in order to keep getting the mild high. This is dangerous because tranylcypromine (see p.30) can be very poisonous when people take more than the prescribed dose; also, because there is a greater risk of adverse interactions with other drugs or substances in food (see p.27). There is a risk of dependency with all MAOIs. This means that people are likely to experience side effects upon withdrawal.

Phenelzine (Nardil)
Form: tablets.
Dose: *Adults:* 15mg three times daily, increased if necessary to four times daily after two weeks. Then reduce to lowest possible maintenance dose; 15mg on alternate days may be enough. Hospital patients may be given a maximum of 30mg three times daily.
Side effects:
Common: dizziness, drowsiness, weakness and fatigue, fluid retention; nausea, vomiting, dry mouth, constipation; inability to sleep, blurred vision, adverse effects on driving ability, low blood pressure when standing up, twitching, muscle spasms, altered liver function and loss of orgasm.
Uncommon: headache, nervousness, excitement, pins and needles, sweating, increased appetite and weight, rash, itching, difficulty urinating, muscle tremor, peripheral neuritis, behavioural changes, arrhythmias, convulsions, impotence and delayed ejaculation, bleeding in the skin, blood disorders, jitteriness, repeating words

very fast, trembling eyes, high blood sodium, glaucoma, lupus-like illness (a condition of the immune system), confusion, hallucinations.
Other: *serious effects which may be very rare and sometimes have been reported in only one patient:* loss of co-ordination, coma (being unconscious), deliriousness, mania (excessive feeling of wellbeing), anxiety, schizophrenia, heart and lung reaction following ECT, jaundice (yellowing of the skin), liver damage which may be serious or even fatal, increased metabolism, swollen glottis (top of the wind-pipe) and fever with increased muscle tension.

Isocarboxazid

Form: tablets.
Dose: *Adults:* 30mg daily initially, in single or divided doses, increased after four weeks if necessary to a maximum of 60mg daily for up to six weeks under close supervision only. Then reduced to usual maintenance dose 10-20mg daily (but 40mg daily may be necessary).
Side effects: see phenelzine (p.29).

Tranylcypromine

Form: tablets.
Dose: *Adults:* 10mg twice daily initially (not later than 3pm), increasing the second dose to 20mg after one week, if necessary. Doses above 30mg daily under close supervision only. Usual maintenance dose 10mg daily.
Side effects: see phenelzine (p.29). Also, insomnia (if given in the evening). Hypertensive crisis (high blood pressure) with a throbbing headache requiring that treatment ends is more likely than with other MAOIs. Liver damage occurs less frequently than with phenelzine.
Withdrawal: because tranylcypromine has a stimulant effect, people may have difficulty coming off it.

Reversible MAOI

Moclobemide (Manerix)

Moclobemide, used for major depression, differs from other MAOIs because it is 'reversible'. This means that there is much less risk of a tyramine crisis arising (see p.27), although the BNF warns against eating large amounts of food high in tyramine (mature cheese, yeast extracts or fermented soya products).

Form: tablets.

Dose: *Adults:* 300mg daily initially, in divided doses after meals, adjusted according to response; usual range 150-600mg daily.

Side effects: sleep disturbance, dizziness, nausea, headache restlessness, agitation, tingling and numbness, dry mouth, visual disturbances, oedema (puffiness), skin reactions. Confusional states have been noticed, which have disappeared rapidly when the drug was stopped; rarely, raised liver enzymes, production of breast milk; low blood sodium.

Drug interactions: may be less likely with moclobemide than with older MAOIs, but you should check with your doctor before taking it with any other medication (including those bought over the counter). Moclobemide should not be given with another antidepressant. Because its effect is short, no treatment-free period is necessary after stopping it. If switching to moclobemide from other antidepressants, leave at least a week's gap before starting moclobemide. The gap should be longer after SSRIs: after paroxetine and sertraline, leave at least two weeks, and after fluoxetine at least five weeks. After taking an older MAOI, leave a week.

Caution: this should not be given to people who are agitated or excited or to people who swing between depression and mania. It should not be given to people with an overactive thyroid, severe liver impairment or anyone acutely confused or with phaeochromocytoma (a rare tumor causing very high blood pressure). Do not use during pregnancy or breastfeeding.

Withdrawal: similar symptoms to tricyclics, see p.22.

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs are a type of antidepressant marketed in the UK since 1989. They block the re-uptake of serotonin into the nerve cell that released it, thereby prolonging its action. These drugs are usually prescribed as the first choice for depression, because they are as effective as the older drugs for most people, and their side effects are usually better tolerated than those of the older drugs and they are less dangerous in overdose. Some of them are also licensed for anxiety conditions and for bulimia nervosa.

SSRIs and people under 18 years old

See above (p.18) for information on NICE guidance on treating depression in this age group. None of these drugs has ever been licensed for children under the age of 18, but they have been widely prescribed for this age group. In December 2003, the MHRA issued guidance stating that no SSRIs should be given to this age group except fluoxetine (Prozac), which should only be given on the advice of a child psychiatrist. Another SSRI should only be used if the child cannot tolerate fluoxetine, again, on the advice of a child psychiatrist. Research evidence suggests paroxetine, sertraline and citalopram are not effective in this age group and are more prone to cause adverse effects, including suicidal feelings, in young people than in adults. (Escitalopram and fluvoxamine have not been studied in this age group.) This guidance also applies to venlafaxine which is an SNRI (see p.41).

Cautions with SSRIs

You should not take SSRIs is you have mania or manic episodes. They should be used with caution in patients with epilepsy (discontinue if fits develop), heart disease, diabetes mellitus, susceptibility to angle-closure glaucoma (a serious eye condition), a history of bleeding disorders (especially gastro-intestinal bleeding), and with other drugs that increase the risk of bleeding; liver or kidney problems, and during pregnancy or breastfeeding. They

should also be used with caution in those receiving ECT at the same time (prolonged fits reported with fluoxetine). The risk of suicidal behaviour is possibly higher in young adults. SSRIs may also affect the performance of skilled tasks such as driving.

Side effects of SSRIs

SSRIs are less sedating and have fewer antimuscarinic effects than tricyclic antidepressants (see p.20), and are less dangerous to the heart and circulatory system. The side effects associated with SSRIs as a group include the following:

Very common: headache, loss of energy, sleepiness, inability to sleep; dry mouth, feeling sick; increased sweating.

Common: migraine, vomiting, diarrhoea, constipation, altered taste sensation, loss of concentration, memory loss, loss of interest in things, nightmares, loss of appetite, weight loss, indigestion, abdominal pain, flatulence, increased salivation, stuffy nose, agitation, loss of libido, anxiety, nervousness, confusion, trembling, ringing in the ears, yawning, itching, muscle and joint pain; tiredness, dizziness, pins and needles.

Uncommon: bleeding into the skin, increased appetite, aggression, feelings of disconnection from surroundings, hallucinations, mania; fainting, dilatation of pupils sometimes associated with glaucoma; changes in heart rate – either faster or slower; itchy rash, hair loss, urinary retention, heavy menstrual bleeding; fluid retention causing puffiness, weight gain.

Rare: increased libido, cough, feeling unwell, sensitivity to sunlight, low blood sodium, fits, movement disorders, liver problems.

Not known: blood disorders; allergic reactions including anaphylactic shock; changes in regulation of urine production; panic attack, tooth grinding; serotonin syndrome (see p.13), restlessness, movement disorders; problems with vision; low blood pressure with changes of position, nose bleeds, internal bleeding, irregular menstrual bleeding; milk secretion in men; abnormal liver function.

Hypomania

Some people may experience hypomania on these drugs, either while taking them or during withdrawal. This may be misinterpreted by doctors who are not aware of the link with the drug, and who may diagnose bipolar disorder and prescribe further medication.

Sexual side effects: these are listed as common

Men: reduced sexual desire, prolonged erection (priapsim - medical advice should be sought urgently), failed erection, delayed ejaculation and lack of orgasm. *Women:* spontaneous orgasm, delayed or inability to reach orgasm or increased libido (with fluvoxamine). Although these effects may be helped by lowering the dose, changing to an alternative drug or stopping the drug for a while, in some people they may persist after the drug has been withdrawn and continue indefinitely. This is a serious concern and if you experience this effect you should report it to the MHRA on a Yellow Card (see *Useful websites* p.52).

Suicide and violence

Suicidal and violent feelings have been experienced not only by people who were being treated for depression but also by people prescribed these drugs for conditions such as chronic fatigue syndrome or back pain, who were not depressed before taking the drugs. It has been suggested that suicidal and violent thoughts associated with SSRIs may be preceded by akathisia – a feeling of restlessness and agitation that causes great unease, and is more commonly associated with antipsychotic medication. If you experience such a sensation while taking an SSRI you should discuss this with your doctor immediately, and be aware of the feelings that may be associated with it.

Suicidal or violent thoughts or actions are also associated, in some reports, with changes in dose (either increases or decreases), and it is important to be aware of this.

Dangerous drug interactions with SSRIs
There are risks if SSRIs are taken with other antidepressants, including MAOIs (or within two weeks of stopping MAOIs). It's essential to have at least a one-week gap after stopping SSRIs before starting MAOIs (with fluoxetine, at least five weeks and for paroxetine and sertraline at least two weeks).

There is evidence of significant adverse interaction between SSRIs and tricyclic antidepressants. With the possible exception of citalopram, all currently available SSRIs may raise the levels of tricyclics in the blood, and therefore increase the risk of serious side effects. Such interactions may occur when drugs are changed from an SSRI to a tricyclic, and this should therefore be done with caution, starting with a low dose of tricyclic and increasing gradually.

Interactions with other psychiatric drugs
There are possible hazards if SSRIs and antipsychotic drugs are prescribed together; in particular: fluoxetine with haloperidol; and fluvoxamine with clozapine. Some SSRIs may increase levels of carbamazepine with risk of carbamazepine levels rising to toxic levels.

Check with your doctor or pharmacist for further information if you are prescribed drugs together, or closely following one another, in case of possible interactions.

Withdrawal from SSRIs
All SSRIs should be withdrawn slowly if possible. The following withdrawal effects are reported: dizziness, numbness, pins and needles, anxiety, disturbed sleep (and vivid dreams), agitation, tremor, nausea, sweating, confusion, depersonalisation (feeling detached from your surroundings), and a feeling of electric shocks or 'head zaps'. The Commission on Human Medicines has received more Yellow Card reports of withdrawal symptoms for paroxetine (Seroxat) than for any other SSRI. This drug has a short half-life (see p.14),

which makes it more difficult to come off. The other drugs in this group with relatively short half-lives are citalopram and sertraline. Fluoxetine (Prozac) has a long half-life, which means it takes a long time for the body to clear the drug completely, and so withdrawal is more gradual than for related drugs. This means that withdrawal from Prozac is usually easier, but also that when problems do occur, they come later in the withdrawal process. For more information on withdrawal, see *Making sense of coming off psychiatric drugs*.

Citalopram (Cipramil)

This drug has been available in the UK since 1995. The active ingredient is escitalopram (see below), which was introduced as a new drug in 2002.

Form: tablets or oral drops.

Dose: *Adults:* 20mg daily as a single dose in the morning or evening, increased if necessary. 40mg tablets available for people with severe depression. For panic disorder, 10mg daily initially, increased to 20mg after one week; usual dose 20-30mg daily. Maximum dose should be 60mg daily. *Older people:* maximum of 40mg daily. 8mg (4 drops) Cipramil® oral drops is equivalent in therapeutic effect to 10mg citalopram tablet.

Side effects: see general SSRIs on p.33.

Caution: see general SSRIs on p.33.

Drug interactions: may have fewer interactions with other drugs than other SSRIs.

Escitalopram (Cipralex)

This was licensed as a new drug in 2002, although it is the active ingredient of citalopram (see above) and so is almost identical.

Form: tablets or oral drops.

Dose: *Adults:* for depression, 10mg daily, increased as necessary to a maximum of 20mg daily. For panic attacks, the starting dose is 5mg, which may be increased to 10mg after one week. Again, the maximum daily dose is 20mg. *Older people:* doses should be halved.

Side effects: see general SSRIs on p.33; in addition: sinusitis, high temperature.
Caution: see general SSRIs on p.33.
Drug interactions: see citalopram (p.36).

Fluoxetine (Oxactin, Prozac, Prozep)

Form: capsules or liquid.
Dose: *Adults:* 20mg daily is generally sufficient for treating depression For the bulimia nervosa – 60mg daily. For obsessive-compulsive disorder – 20mg daily initially; if there is no response after several weeks, the dose may be increased but this may result in more side effects. Maximum dose 60mg daily.
Side effects: see general SSRIs on p.33; frequency of different side effects is not reported for fluoxetine. Also dilatation of blood vessels, sore throat, breathing problems, chills, changes in blood sugar, increased urinary frequency; rarely lung disease; very rarely a condition similar to neuroleptic malignant syndrome (see p.13 and *Making sense of antipsychotics*).
Drug interactions: MAOIs – see p.28.

Fluvoxamine (Faverin)

Form: tablets.
Dose: *Adults:* 100mg daily up to a maximum of 300mg daily (over 100mg daily should be given in divided doses). Fluvoxamine can also be given for obsessive-compulsive disorder, but if there is no improvement within 10 weeks, it should be reviewed.
Side effects: palpitations, fast heart rate (may also cause slow heart rate); rarely low blood pressure on standing, confusion, unsteadiness, tingling, feeling unwell, taste disturbance, a condition similar to neuroleptic malignant syndrome (see p.13), abnormal liver function.
Drug interactions: see fluoxetine, and general SSRIs on p.33. It also interacts with the asthma drugs theophylline and aminophylline. Consult your doctor or pharmacist if this applies.
Withdrawal: avoid abrupt withdrawal.

Paroxetine (Seroxat)
Form: tablets or liquid.
Dose: *Adults:* 20mg daily, increasing, if necessary, by 10mg stages to a maximum of 50mg daily. Normally taken in the morning. For obsessive-compulsive disorder (OCD): 20mg each morning, initially increasing by 10mg stages weekly to a usual dose of 40mg and a maximum dose of 60mg. For panic disorder: as for OCD, but maximum of 50mg. *Older people:* 20mg daily up to a maximum of 40mg.
Side effects: see general SSRI information on p.33. Also: raised cholesterol; less commonly: changes to heart rhythm, brief changes in blood pressure, confusion, urinary incontinence; rarely: panic attacks and increased anxiety during initial treatment of panic disorder (reduce dose), depersonalisation (feeling out of touch with your surroundings), and neuroleptic malignant syndrome-like event (see above p.13). The Commission on Human Medicines has received more reports of involuntary movements of mouth and face for paroxetine than for other SSRIs.
Drug interactions: see general SSRIs on p.35.

Sertraline (Lustral)
Form: tablets.
Dose: *Adults:* 50mg daily initially, increased if necessary in 50mg stages over several weeks to a maximum dose of 200mg daily, then reduced to usual maintenance dose of 50mg daily. Doses of 150mg or more should not be used for more than eight weeks.
Side effects: see general SSRIs on p.33. Also: sore throat, colds and ear infection; nightmares and sleep walking; pancreatitis, hepatitis, jaundice, liver failure, memory problems, urinary incontinence, more marked movement disorders and eye problems, breathing problems and hiccups, tongue and mouth disorders including mouth ulcers; anal bleeding. Sertraline has been shown to be safe for people with unstable angina or who have had a recent heart attack.
Drug interactions: see general SSRIs on p.35.

Serotonin and noradrenaline reuptake inhibitors (SNRIs)

These drugs share many of the characteristics of SSRIs. They slow the re-uptake of both noradrenaline and serotonin and thus prolong their action; but they have a more selective action than the tricyclics. They should not be taken at the same time as other antidepressants, including St John's wort.

Duloxetine (Cymbalta)

Duloxetine was licensed for the treatment of major depression in the UK in December 2004. It is also used for treating other conditions, including stress incontinence. When used for stress incontinence, it has a different trade name, which is Yentreve. You should not take two different formulations of duloxetine at the same time. A review of the evidence for duloxetine in the 2007 *Drug and Therapeutics Bulletin* concluded that there is no place for duloxetine in the treatment of depression.

Form: capsules.

Dose: *Adults:* the recommended starting and maintenance dose is 60mg daily. Higher doses can be given, but there is no evidence that they will be more effective in patients who do not respond to the starting dose. *Older people:* there is only limited information on the use of duloxetine in older people, who should therefore be treated with caution. It is not recommended for people over the age of 75.

Side effects:

Very common: nausea, headache, dry mouth, extreme sleepiness and dizziness.

Common: loss of appetite; inability to sleep, agitation, decreased libido, anxiety, abnormal orgasm, abnormal dreams; trembling, pins and needles; blurred vision, ringing in the ears, palpitations; flushing, yawning; constipation, diarrhoea, vomiting, indigestion, flatulence; increased sweating, rash; muscle pain, muscle spasms and tension; problems with erection; fatigue, abdominal pain, weight loss.

Uncommon: laryngitis; raised blood sugar; sleep problems, tooth grinding, disorientation, loss of interest in things; nervousness, loss

of concentration, lethargy, disturbed taste sensation, movement disorder, restless legs syndrome; dilated pupils, sight problems; vertigo, ear pain; fast heart rate, disturbances of heart rhythm; raised blood pressure; cold hands and feet, low blood pressure on standing up, fainting; tight throat; nose bleed; upset stomach, belching, inflammation of the stomach; liver problems; night sweats, itchy rash, dermatitis, cold sweats, increased sensitivity to sunlight, increased tendency to bruise; muscle twitching; urinary retention, problems with urination including frequency and needing to go at night, reduced urine flow; problems with ejaculation, menstrual irregularities; feeling strange, feeling cold, thirst, feeling unwell, feeling hot, disturbed gait, weight gain.

Rare: allergic and sensitivity reactions, reduced thyroid function; dehydration, low blood sodium, mania, hallucinations, aggression and anger; fits; glaucoma; sore mouth, breath odour, anal bleeding; lockjaw; strange smelling urine; menopausal symptoms; milk secretion; high blood prolactin; raised cholesterol.

Not known: movement disorders and restlessness; very high blood pressure; internal bleeding, jaundice, liver failure; severe allergic reaction causing swelling of nose and throat; severe skin rash spreading to major organs, chest pain.

Caution: should not be given to people with impaired liver function, nor those with severe kidney disease. It should be used with caution in people with a history of mania or bipolar disorder or fits; with increased pressure in the eyes, or glaucoma; with high blood pressure or heart disease – blood pressure should be monitored in these cases; taking anticoagulant drugs such as warfarin.

Drug interactions: its use with other psychiatric drugs has not been evaluated, so it should be used with caution with other substances which affect the brain, including alcohol and sedative drugs such as benzodiazepines (minor tranquillisers), morphine-related drugs, antipsychotics, phenobarbital, and antihistamine sleeping pills.

Withdrawal: common withdrawal symptoms, especially if it is stopped abruptly, include dizziness, nausea, insomnia, headache,

and anxiety. The mean half-life of duloxetine is longer than venlafaxine and paroxetine, but shorter than fluoxetine (Prozac).

Venlafaxine (Efexor, Efexor XL, Bonilux XL, Foraven XL, Politid XL, Ranfaxine XL, Tifaxin XL, Venlalic XL, Venaxx XL, Vensir XL, Winfex XL)

At doses of up to 150mg, venlafaxine acts in the same way as the SSRIs, and is therefore often included in that group. At higher doses it also inhibits noradrenaline.

Form: tablets or capsules.

Dose: *Adults:* 75mg daily initially, in two divided doses, increased if necessary after several weeks to 150mg daily in two divided doses. For severe depression (and those in hospital) 150mg daily initially in two divided doses, increased if necessary in steps of up to 75mg every two to three days to a maximum of 375mg daily. The XL names refer to modified release formulations which mean that the daily dose can be taken all at once. Dose for these: 75mg once daily, increased if necessary after at least two weeks to 150mg once daily; max. 375mg once daily. For anxiety disorders, the maximum dose is 225mg. Best taken at the same time each day.

Side effects:

Very common: nausea, dry mouth, headache and sweating (including night sweats).

Common: raised cholesterol, weight loss; abnormal dreams, decreased libido, dizziness, increased muscle tone, loss of sleep, nervousness, pins and needles, sedation, trembling, confusion, feeling disconnected from surroundings; sight problems, dilated pupils; high blood pressure, dilated blood vessels causing hot flushes, palpitations; yawning; loss of appetite, constipation, vomiting; difficulty urinating; sexual problems including abnormal ejaculation/orgasm, inability to reach orgasm, impotence, menstrual problems such as increased bleeding or irregular bleeding, very frequent urination; lack of energy, chills.

Uncommon: bleeding in skin or intestines; weight gain; loss of interest is things, hallucinations, muscle spasms, agitation, loss of

coordination and balance; altered taste sensation, ringing in ears; low blood pressure on standing up, fast heart rate, fainting; diarrhoea; tooth grinding; rash, hair loss; sensitivity to sunlight.
Rare: restlessness, fits, mania.
Frequency unknown: bleeding and blood disorders; disturbances of liver function; low blood sodium; raised prolactin (may stimulate breast development and milk production); movement disorders including involuntary movements; disorders of heart rhythm; low blood pressure, pancreatitis; severe allergic reactions; anaphylaxis, blood diseases, muscle break-down.
Caution: should be used with caution in people who have had a heart attack or have unstable heart disease (blood pressure should be monitored if taking more than 200mg daily), in people with a history of epilepsy, liver or kidney disease and in those who have abused drugs. It should not be given to those with severe kidney or liver disease, or in pregnancy or while breastfeeding. Driving and other skilled tasks may be affected.
Withdrawal: this drug has a very short half-life so withdrawal is often difficult and should be done slowly. Withdrawal symptoms include: dizziness, vertigo, nausea, lightheadedness, fatigue, headache, insomnia, agitation, abdominal cramps, chills, and shock-like sensations. It should be no more difficult to come off the modified release than the standard form.

Other antidepressants

Agomelatine (Valdoxan)

Agomelatine was first licensed in 2009, for major depression in adults. It works differently from other antidepressants, promoting the action of melatonin, a hormone which is involved in regulating the body's response to day length and associated biorhythms. It increases levels of two neurotransmitters, noradenaline and dopamine, in the front part of the brain, and it does not affect levels of serotonin.

Form: tablets.
Dose: 25mg taken at bedtime.
Side effects:
Common: headache, dizziness, somnolence, insomnia, migraine; anxiety; nausea, diarrhoea, constipation, upper abdominal pain; excessive sweating; back pain; tiredness, disturbed liver function.
Uncommon: pins and needles; blurred vision; eczema.
Rare: red rash; hepatitis (liver disease).
Frequency unknown: suicidal thoughts or behaviour; agitation.
Cautions: you should receive a liver function test before you start taking agomelatine and at 6, 12 and 24 weeks after starting, and after that as necessary. It should be used with caution in people over 65, those with kidney disease, those with a history of manic episodes. It should not be used for children, or people with dementia. Its safety in pregnancy is not known, and it should not be taken while breastfeeding. You should not drink alcohol while taking it. It contains lactose and should not be taken by people with lactose intolerance. Interactions: you should not take agomelatine with fluvoxamine and should be cautious about taking it with drugs containing oestrogen, or with propranolol.

Mirtazapine (Zispin Soltab)

Mirtazapine is licensed for major depression. The BNF suggests it should be tried if someone has not responded well to SSRIs. It is similar to the tricyclics, in that it affects both the noradrenaline and the serotonin systems, but it is more selective, stimulating only one type of serotonin receptor. It has few antimuscarinic effects (see p.20) but causes sedation at the start of treatment.
Form: tablets or liquid. Zispin Soltab is a rapidly dissolving tablet which also contains the sweetener aspartame.
Dose: *Adults and older people:* 15mg daily initially, increasing according to response up to 45mg daily as a single dose at bedtime or in two divided doses.

Side effects:

Very common: increased appetite and weight gain; sleepiness, sedation, headache; dry mouth.

Common: abnormal dreams, confusion, anxiety, insomnia; feeling lethargic, dizziness, shaking; low blood pressure on standing; feeling sick, diarrhoea, vomiting; rash; joint pain, muscle pain, back pain; oedema (fluid retention causing puffiness), fatigue.

Uncommon: nightmares, mania agitation, hallucinations, restlessness and inability to sit still; pins and needles, restless legs, fainting; low blood pressure; loss of sensation in the mouth.

Rare: muscle spasms; changes in liver function.

Not known: blood disorders making you more likely to get infections; suicide and suicidal feelings; low blood sodium, fits, serotonin syndrome (see above pXX), mouth swelling; severe rashes leading to severe illness.

Caution: avoid in pregnancy and breastfeeding. Should be avoided or used with caution in people who have epilepsy, liver or kidney disease, low blood pressure, a history of urinary retention, angle-closure glaucoma, diabetes mellitus, psychotic illnesses, and a history of bipolar disorder. You should report any fever, sore throat, mouth ulcers or other signs of infection during treatment, and blood tests should be carried out. If patients become jaundiced, treatment should not continue.

Withdrawal: avoid abrupt withdrawal.

Reboxetine (Edronax)

Reboxetine is licensed for major depression and is supposed to act more quickly than other antidepressants, although the evidence for this is weak. It may have fewer antimuscarinic effects. It's suggested that it may suit those who have not responded to, or who can't tolerate, SSRIs or tricyclic antidepressants.

Research published in October 2010, analysing both published and previously unpublished drug trial results, said that all the trials taken

together showed that reboxetine was less effective than placebo (a dummy pill) for depression, and its possible harms outweighed its benefits.

Form: tablets.

Dose: *Adults:* 4mg twice daily, increased if necessary after three to four weeks to 10mg daily in divided doses, to a maximum of 12mg daily.

Side effects:

Very common: insomnia; dry mouth, constipation; sweating.

Common: vertigo; tachycardia, palpitation, vasodilation, postural hypotension; abnormality of accommodation; lack or loss of appetite; urinary hesitancy, sensation of incomplete bladder emptying, urinary tract infection; erectile dysfunction (males only), ejaculatory pain (males only), ejaculatory delay (males only), testicular disorder-primarily pain (males only); chills.

Not known: agitation, anxiety, irritability, aggressive behaviour, hallucinations, nausea, vomiting, allergic dermatitis/rash, pins and needles, hypertension, bad circulation in hands and feet, low blood sodium; testicular pain.

Drug interactions: reboxetine should not be started until two weeks after stopping a MAOI antidepressant, and a MAOI should not be started until at least one week after stopping reboxetine. Manufacturers advise against its use with heart drugs, antipsychotics, tricyclic antidepressants, cyclosporin, and some antifungal drugs and antibiotics. It's very important your doctor knows about all of the medications you are taking (including over-the-counter remedies). Its use with other antidepressants has not been evaluated.

Caution: not recommended for older people. Reboxetine should be avoided or used with caution in people with severe kidney disease, liver disease, bipolar disorder, a history of epilepsy, urinary retention and glaucoma. It should be avoided in pregnancy and while breastfeeding.

Tryptophan/L-tryptophan (Optimax)
Tryptophan is an amino acid present in the normal diet in small quantities and therefore may be seen as a food supplement rather than a drug. But it has been used very cautiously in psychiatry, since it was associated with an outbreak of severe disease (eosinophilia myalgia syndrome) in America in 1989, almost certainly due to contamination during the production process at the time, rather than the drug itself.

The BNF recommends that it should be used in addition to other antidepressants, and started by a specialist. Prescription may then be continued by your GP.
Form: tablets.
Dose: *Adults:* 1g three times daily to a maximum of 6g daily. *Older people:* a lower dose may be appropriate, especially for those with kidney or liver disease.
Side effects: Slight nausea which usually disappears within 2 or 3 days, and can be minimised by taking L-tryptophan after food; headache; light-headedness. Eosinophilia myalgia syndrome is a blood disorder bringing severe muscle pain, joint pain, fever, swelling and skin rash, which may involve the lungs and central nervous system. Because it was in the past associated with tryptophan (see above), the manufacturer recommends you should have blood tests and be monitored for any muscular symptoms.
Drug interactions: combining tryptophan and SSRIs may cause agitation and nausea, and it should also be used with caution with MAIOs or duloxetine.
Caution: It should not be used in pregnancy or while breastfeeding.

Compound drugs

Sometimes drugs are made which combine two or more medicines into one tablet. Because the doses of each separate drug can't be adjusted to individual needs, it may be preferable to take the two

kinds of drugs separately. If you have been taking a combination drug for more than a few months, you should ask your doctor to take a fresh look at your needs.

Triptafen

This combines an antidepressant with an antipsychotic at these doses: 25mg amitriptyline hydrochloride; 2mg perphenazine.

The dose of perphenazine is low and considered unlikely to cause the severe side effects associated with antipsychotic drugs. If you experience muscle spasms, or tics or effects which mimic Parkinson's disease, such as tremor, stiffness or involuntary movements, while taking Triptafen, you should talk to your doctor about either changing the drug or taking something in addition to help these symptoms. For more information about perphenazine, see *Making sense of antipsychotics* (Mind, 2011).

Other drugs used to treat depression

If you have severe depression which is not responding to antidepressants, you may be offered an alternative or an additional drug.

Lithium (Camcolit, Liskonum, Priadel)

Lithium is mainly used for bipolar disorder, but may also be given as a preventive therapy if you have repeated episodes of severe depression. (See *Making sense of lithium and other mood stabilisers,* Mind, 2011.)

Quetiapine (Seroquel XL)

The antipsychotic quetiapine has also been licensed for depression in bipolar disorder and to supplement antidepressants in severe depression. For more information about quetiapine see *Making sense of antipsychotics* (Mind, 2011).

Flupentixol (Fluanxol, Depixol)
This is a low-dose preparation of an antipsychotic, which is used in higher doses to treat severe mental distress such as schizophrenia. It should be used for short-term treatment only. As this drug tends to take effect quickly, if there is no improvement within one week, manufacturers advise that treatment be stopped.
Form: tablets.
Dose: *Adults:* 1mg initially in the morning, increasing after one week to 2mg if necessary. Maximum dose 3mg daily in divided doses, not later than 4pm. *Older people:* 0.5mg initially, increasing to 1mg if necessary. Maximum 2mg daily in divided doses, not later than 4pm.
Side effects: restlessness, insomnia, and overactive and excitable behaviour. *Rarely:* dizziness, tremor, visual disturbances, headache, raised blood prolactin levels (a hormone involved in producing breast milk), movement disorders, suicidal behaviour. If movement disorders occur, the drug should be stopped.
Drug interactions: unwanted effects may be increased if given with other antidepressants. Sedation will increase if it is taken with sleeping pills or anti-anxiety drugs. Avoid alcohol as this also provokes drowsiness.
Caution: skilled tasks such as driving can be affected. Should be avoided in excitable, overactive or manic people and used with caution in people with Parkinson's disease, liver, kidney or heart disease or dementia.
Withdrawal: should be stopped gradually.

What other treatments are there?
The NICE guidance on depression suggests that depression may get better without treatment, and that in less severe cases talking therapies such as CBT, and exercise, especially outdoors, may be more helpful than antidepressants.

For anxiety, NICE suggests that you should receive CBT first, and drug treatment or self help strategies if CBT doesn't work for you.

Many people find complementary and alternative treatments helpful, including reflexology, homeopathy, herbal medicine, aromatherapy, meditation, and various forms of meditative exercise such as yoga or tai chi. When using these therapies and techniques, it is important to work with a qualified and experienced practitioner who is able to offer support appropriate for mental health issues.

Index of drug names

Useful organisations

Mind
Mind works in England and Wales, providing local services and campaigning for change to enable people with experience of mental distress to have a better quality of life.
website: www.mind.org.uk
email: info@mind.org.uk
Mindinfoline on 0300 123 3393 (Monday to Friday, 9am to 5pm)

British Association for Behavioural and Cognitive Psychotherapies (BABCP)
Can provide details of accredited therapists
tel. 0161 797 4484
web: www.babcp.com

British Association for Counselling and Psychotherapy (BACP)
For details of local practitioners
tel. 01455 883 300 (general enquiries)
tel. 0870 443 5220 (to find a therapist)
web: www.bacp.co.uk

Carers UK
Information and advice on all aspects of caring
helpline: 0808 808 7777
tel. 020 7922 8000
web: www.carersuk.org

MDF The Bipolar Organisation
Works to enable people affected by manic depression to take control of their lives
tel. 08456 340 540
web: www.mdf.org.uk

Medicines and Healthcare products Regulatory Agency (MHRA) (and Commission on Human Medicines)
See their website for documents on taking medicines
tel. 020 7084 2000
web: www.mhra.gov.uk

UK Council for Psychotherapy (UKCP)
Maintains a voluntary register of qualified psychotherapists
tel. 020 7014 9955
web: www.psychotherapy.org.uk

Useful organisations

Yellow Card Scheme
For reporting side effects and withdrawal effects of drugs. Also has a translation service for those whose first language is not English
hotline: 0808 100 3352 (business hours)
web: www.yellowcard.gov.uk

Useful websites

www.depressionalliance.org
Information about depression and local self help groups

www.dh.gov.uk
For the MHRA *Medicines use review: understand your medicines* leaflet.

http://emc.medicines.org.uk
Electronic *Medicines Compendium* – for Patient Information Leaflets and data sheets on most prescribed drugs.

http://medguides.medicines.org.uk
Medicines Information Project for details on individual drugs

Further information

Mind offers a range of mental health information, covering:

- diagnoses
- treatments
- wellbeing

Mind's information is ideal for anyone looking for further information on any of these topics.

For more details, contact us on:

tel: 0844 448 4448
email: publications@mind.org.uk
web: www.mind.org.uk/shop
fax: 020 8534 6399

Support Mind

Providing information costs money. We really value donations, which enable us to get our information to more people who need it.

Just £5 could help another 15 people in need receive essential information booklets.

If you would like to support our work with a donation, please contact us on:

tel: 020 8215 2243
email: dons@mind.org.uk
web: www.mind.org.uk/donate

Mind's mission

- Our vision is of a society that promotes and protects good mental health for all, and that treats people with experience of mental distress fairly, positively, and with respect.
- The needs and experiences of people with mental distress drive our work and we make sure their voice is heard by those who influence change.
- Our independence gives us the freedom to stand up and speak out on the real issues that affect daily lives.
- We provide information and support, campaign to improve policy and attitudes and, in partnership with independent local Mind associations, develop local services.
- We do all this to make it possible for people who experience mental distress to live full lives, and play their full part in society.

Contact us using Mind Infoline on 0300 123 3393 or email info@mind.org.uk Monday to Friday 9am to 5pm. We can give you details of Mind and other services local to you. We use Language Line if you want to talk to us in a language other than English.

Mind covers England and Wales. For Scotland call the Scottish Association for Mental Health tel. 0141 568 7000 or for Northern Ireland contact the Northern Ireland Association for Mental Health tel. 028 9032 8474.

mind

For better mental health