



For better
mental health

Making sense of antidepressants



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Making sense of antidepressants

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 these drugs?

Drug names

Drugs can have two types of name: 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.

Informed consent

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, likely effects and risks of the treatment, including its chance of success, and any alternatives to it. Generally, you can only receive treatment that you have specifically agreed to. Once you have given your consent, it isn't final and you can always change your mind. This consent to treatment is fundamental, and treatment given without it can amount to assault and negligence. However, there are times when treatment can be given without consent – see *Mind rights guide 3: consent to medical treatment*, under *Further reading* on p. 50, for more details.

Patient information leaflets

If you are prescribed medication as an outpatient, or from 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 is usually a very small piece of paper), 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; 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 and when; possible side effects; the expiry date of the drugs and how to store them.

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.

Some of the information is quite hard to understand, and the Commission on Human Medicines (formerly the Committee on Safety of Medicines) has been looking at ways of making it easier. They have produced a leaflet *Taking medicines – some questions and answers about side effects* which you can find on their website or request by telephone, or may be available in your local pharmacy. There is more information on medicines and their use, in the form of Medicines Guides, available from

the Medicines Information Project website (See *Useful organisations* on p. 48 for details of both these organisations.) 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.

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?
- Can I take them with other drugs I have been prescribed?
- 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?
- 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 (this is when a 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 some high-street chemists have space set aside where you can talk privately.

Since January 2006, a new scheme has been in place called the 'Medicines Use Review'. People who regularly take more than one prescription medicine, or take medicines for a long-term illness, are encouraged to go to pharmacists who are operating the scheme, for a full discussion of their medicines and any problems they may have with them. The Medicines and Healthcare products Regulatory Agency (MHRA), who are responsible for overseeing the licensing of medicines, have produced a guide to the scheme which is available on the Department of Health website. (See *Useful websites* on p. 49.)

What are the causes of depression?

There are a number of theories about the causes of depression; social, psychological and physical factors all play their part. Very often, doctors tell people with depression that they are suffering from a 'chemical imbalance'; but this is a fairly meaningless phrase, as there is no real evidence for it. The only evidence is that medication which is designed to change the chemistry in particular ways does often lift the depression, but the real effect of chemicals on the brain is extremely sophisticated and complicated, and still not properly understood. Talking of 'chemical imbalance' not only implies a better understanding than we have, but also ignores what may have caused the supposed imbalance in the first place.

Many people know exactly why they are depressed, and can talk about the life events that preceded it; but they may need some medication to help them to cope while they recover and adjust. Medication alone rarely provides a complete solution. Further information on depression, its causes and the different treatment options can be found in Mind's booklet *Understanding depression*.

What treatments are used for depression?

Drugs and electroconvulsive therapy (ECT) are often the only form of help offered to people diagnosed with depression. The most common treatment, by far, is antidepressant drugs. Antipsychotic drugs and amino acids have also been used in the treatment of depression (see p. 43 for more details).

In December 2004, the National Institute for Health and Clinical Excellence (NICE) published guidelines on the treatment of depression. These suggest that antidepressants should not be used as a first treatment for mild to moderate depression, and that other treatments should be offered, including talking treatments and exercise regimes, which may be as effective as drug treatment. It also suggests 'watchful waiting' – recognition of the fact that depression sometimes just goes away without any medical intervention, and that active treatment may be unnecessary. The guidelines suggest that when an antidepressant is prescribed, it should be an SSRI (see p. 30), because their side effects are better tolerated than those of the alternative antidepressants.

The BNF (*British National Formulary*) suggests that antidepressants are helpful especially when moderate to severe depression is causing loss of appetite and difficulty sleeping.

A herbal remedy, St John's wort (*Hypericum perforatum*) has been found helpful for mild to moderate depression. It's worth remembering, however, that many standard medicines are based on plant extracts, and just because something is a herb, it doesn't mean that it's necessarily safer than other medicines, or free from side effects. Do not take St John's wort with other antidepressants, as there is evidence of adverse interactions. It also has serious interactions with other drugs. (See Mind's web-based factsheet *St John's wort*.)

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 terminated by being taken back up into the neuron that released them (re-uptake). 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 their actions in one part of the brain will also cause side effects because of their interference on the same neurotransmitters in other parts of the body and brain. As we learn more about the specific actions of different neurotransmitters, we can classify their receptors into different subtypes, depending on what response they trigger; for example, noradrenaline receptors are classified as alpha and beta receptors. Many people are familiar with the term 'beta blockers' – these drugs block beta receptors and therefore reduce the effect of noradrenaline at these sites. In designing new antidepressants, the aim is usually to target the drug only on brain receptors thought to be directly involved with depression, to avoid changing the action of the neurotransmitter at other sites.

How effective are antidepressants?

Psychiatric research indicates that:

- Antidepressants can be effective for 70 per cent of people who have them prescribed. However, the value of these findings is weakened by the fact that in 40 per cent of people, a dummy drug (placebo) is just as effective. In other words, the psychological impact of just being given something that's meant to help you appears to be beneficial. Moreover, the advantage of antidepressants over placebo may be exaggerated by the research methods used, and positive results are much more likely to be published than negative results.
- Recent reviews of groups of research studies suggest that SSRIs are no more effective than a dummy drug.
- In milder depressions, short-term psychotherapy (a talking treatment) is as effective as drugs (see *Understanding talking treatments*).
- The evidence that antidepressants are more effective in severe depression is weak.
- One study comparing standard GP care, drug treatment from a psychiatrist, cognitive behaviour therapy (a particular type of talking treatment) and social work counselling found that specialist referral, particularly for cognitive behaviour therapy, produced the best results.
- 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.

How long do they take to start working?

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. However, it has been suggested that for people who have not found an antidepressant helpful, this approach might be worth trying, perhaps before resorting to lithium or 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?

A significant number of 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 can 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.

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, if necessary by letter. 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 system (see *Useful Organisations*).

There is a warning from the Commission on Human Medicines about low blood sodium levels (hyponatraemia) associated with all antidepressants. This mainly affects older people. Signs are drowsiness, confusion or convulsions.

Antidepressants may affect driving and other skilled tasks.

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.

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 been associated with SSRI antidepressants, with many published anecdotes, but there is a suggestion that the same thing may occur with other types of antidepressants too. 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. 31) in relation to SSRI antidepressants in particular.

The BNF (*British National Formulary*) 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.

How long should I stay on antidepressants?

Studies show that staying on antidepressants for six months after they have become effective can help prevent further episodes of depression. Some studies suggest that most people aren't being given sufficient antidepressants for long enough. The BNF (*British National Formulary*) recommends that people should be maintained at the effective dose for at least six months (about 12 months in older people) after the depression has lifted. If treatment stops too soon, the depression is likely to come back. In recurrent depression, maintenance therapy with an effective dose may need to continue for several years (information about 'maintenance' doses is included under the individual drugs).

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 other professional how long to remain on your antidepressants and how to go about stopping them.

How easy is it to come off them?

Withdrawal reactions can occur with all major types of antidepressant. Problems are more likely to occur after abrupt withdrawal and longer courses of treatment. Reactions usually start suddenly within a few days of stopping the antidepressant, or of reducing its dose. Individuals vary in their susceptibility to withdrawal problems, and while some people may stop taking their drugs with no problems, 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. 49 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 resemble having electric shocks.

The BNF (*British National Formulary*) 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. Some reports

suggest that gradually reducing the dose may not be necessary when switching between SSRIs; but if withdrawal symptoms are severe, the antidepressant may need to be restarted and the dose reduced more gradually. Some drugs are available in liquid form and this means that the dose can be more easily reduced very gradually by repeated dilution.

A listing 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 happen 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. 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.

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. People can get slightly high from the stimulant effect of the monoamine oxidase inhibitor (MAOI) antidepressant tranylcypromine. A few people take larger doses than prescribed in order to keep getting the mild high. This is dangerous because tranylcypromine (see p. 28) 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. 26). There is a risk of dependency with all MAOIs. (This means that people are likely to experience side effects upon withdrawal.)

In a very useful summary of the whole issue of 'addiction to' or 'dependence on' antidepressant drugs, the American psychiatrist, Joseph Glenmullen, has written, 'Not all patients who develop withdrawal symptoms become addicted, or dependent. Addiction occurs when patients suffer such intolerable or incapacitating withdrawal symptoms that they are forced to restart the drugs, put the dose back up, or taper them off more slowly. Patients are then dependent on antidepressants for as long as it takes to wean off the drugs. Dependence and addiction are the same things: dependence being the technical medical term used by doctors and addiction the plain English term used by patients.'

When shouldn't I take antidepressants?

Pregnant and nursing mothers

Although few drugs have been proved to cause birth defects, great caution is necessary with drugs during pregnancy. A balance has to be struck between the needs of the mother-to-be and the possible risk to the unborn child, particularly in the first three months of pregnancy.

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. Recently published research suggests that taking SSRIs in pregnancy may be associated with an increase in the likelihood of birth defects, especially heart problems 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, as less is known about them. Doxepin (Sinepin), in particular, should be avoided in breastfeeding.

When a woman who is pregnant or who is breastfeeding is suffering from depression, every alternative to drugs should be explored. 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 these are refused.

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

Drug interactions

If you are prescribed antidepressants, it's important to inform your doctor about any other drugs you are taking, 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 a significant contributor to the depression 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.

The different types of antidepressant

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. 49). It is very dangerous to exceed 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) noradrenaline and serotonin. Related drugs (mianserin and trazodone, see p. 24) have a similar chemical structure and action to the tricyclics, but differ in their adverse effects: the tricyclic drugs have a broader chemical action and also affect a third transmitter system, causing side effects to the heart and circulatory 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 someone is feeling agitated and having difficulty sleeping, a sedating antidepressant may be most helpful. Those which are more sedating include amitriptyline, clomipramine, dosulepin (dothiepin), doxepin, mianserin, trazodone, and trimipramine, while the less sedating ones are imipramine, lofepramine, and nortriptyline.

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, gradual introduction is very important.

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.

Special difficulties arise when these antidepressants are used in the treatment of psychosis. If given to people with epilepsy, this group of antidepressants can make people more likely to have fits, and they should not be used in conjunction with ECT or with anaesthetics.

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

Drug interactions with tricyclics

If this group of antidepressants is taken with some antipsychotics, such as chlorpromazine (Largactil) the adverse effects can become much worse. If they are taken with minor tranquillisers or sleeping pills, such as diazepam (Valium), the sedative effect increases. This group of drugs should not be taken for at least two weeks after stopping MAOI antidepressants (see p. 27).

There is also evidence of significant adverse interaction between tricyclics and SSRIs (see p. 31 for more details). If you are taking any other drugs you should discuss this with your doctor.

Withdrawal from tricyclics

Cutting the dose down gradually will help minimise any withdrawal symptoms. People withdrawing may experience the following more common symptoms: a flu-like pattern, 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 may occur, and difficulty getting to sleep, followed by very vivid dreams early in the night, which can be frightening. People may experience general restlessness. 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 compounds Triptafen and Triptafen-M, combined with the antipsychotic, perphenazine)

Form: tablets or liquid.

Adult dose: 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:** (commonest 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.

Adult dose: 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:** see amitriptyline; also diarrhoea; hair loss. **Drug interactions:** see MAOIs on p. 27.

Dosulepin/dothiepin (Prothiaden)

Form: tablets or capsules.

Adult dose: 75mg daily initially, increased as necessary up to a maximum 150mg daily.

Older people: 50-75mg. **Side effects:** see amitriptyline.

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.

Adult dose: 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. **Caution:** avoid while breastfeeding.

Imipramine

Form: tablets.

Adult dose: 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. **Withdrawal:** studies show that 21 to 55 per cent of people experience gastric and other bodily discomforts.

Lofepramine (Feprapax, Lomont)

Form: tablets or liquid.

Adult dose: 140-210mg daily in divided doses. **Older people:** older people may respond to lower doses. **Side effects:** like amitriptyline, 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.

Adult dose: 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, but less sedating.

Trimipramine (Surmontil)

Form: tablets or capsules.

Adult dose: 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.

Adult dose: 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.

Adult dose: 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, 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 the drug should immediately be stopped and medical advice sought.

Noradrenergic and specific serotonergic antidepressant (NaSSA)

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 but causes sedation at the start of treatment.

Form: tablets or liquid. Zispin Soltab comes as rapidly dissolving tablets which also contain the sweetener aspartame.

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:** (most common) increased appetite and weight gain, oedema (fluid retention causing puffiness), sedation; less commonly dizziness, headache; rarely low blood pressure on standing, abnormal dreams, mania, suicidal behaviour, fits, shaking, muscle spasms, tingling, joint pains, muscle pains, restlessness, rash, and reversible blood disorders; very rarely angle-closure glaucoma (a serious eye condition). **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. Patients 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.

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 of them are released. Because of their side effects, fewer MAOIs tend to be prescribed and, usually, when other antidepressants (tricyclics or SSRIs) have failed; and 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 will 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: matured cheeses; game; protein and yeast extracts such as Marmite, Bovril or Oxo; alcohol (especially red wine); non-alcoholic beer and lager; overripe fruits; broad bean pods and 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 are prone to agitation 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.

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.
- Buspirone (Buspar) given for anxiety.
- Carbamazepine (Tegretol) given for manic depression or epilepsy.
- Barbiturates because their effects may be heightened.
- Certain antipsychotic drugs (major tranquillisers) 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. 21). 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.

Phenelzine (Nardil)

Form: tablets.

Adult dose: 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:** (commonest first) low blood pressure on standing and dizziness. Drowsiness, insomnia, headache, weakness and tiredness, dry mouth, constipation and other gastric disturbances, oedema (puffiness), muscle spasms and jerks, raised liver enzymes, agitation and tremors, nervousness, feelings of excitement, disturbances of heart rhythm, blurred vision, wobbling eye movement, difficulty in passing water, sweating, fits, rashes, blood disorders, interference with sexual function, weight gain with appetite changes. Psychotic episodes with mania, confusion and hallucinations, suicidal behaviour. Rarely, jaundice and severe liver poisoning, tingling in hands and feet, low blood sodium.

Isocarboxazid

Form: tablets.

Adult dose: 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.

Tranlycypromine

Form: tablets.

Adult dose: 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. 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, derives from the MAOI group, but differs from others because it is 'reversible'. This means that there is much less risk of a tyramine crisis arising (see p. 26), although the BNF warns against eating large amounts of food high in tyramine (mature cheese, yeast extracts or fermented soya products).

Form: tablets.

Adult dose: 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, and 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 than with older MAOIs, but patients should check with their 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. However, leave at least a week's gap before starting moclobemide after taking tricyclics, SSRIs, or related antidepressants. (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. 21.

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 although they have at least as many possible side effects listed in the BNF, they are usually better tolerated than the older drugs and 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. 17) 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. Only if a child can't tolerate fluoxetine can another SSRI be used; 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 side 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 (see p. 39).

Cautions with SSRIs

SSRIs should not be used for someone with mania. 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 breast-feeding. 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. 19), and are less dangerous to the heart and circulatory system. The most common side effects include gastric disturbance, such as nausea, vomiting, indigestion, abdominal pain, diarrhoea, constipation; appetite and weight changes (both loss of appetite with weight loss increased appetite and weight gain are reported); hypersensitivity reactions including rash (which may be sign of a serious systemic reaction starting which may affect the whole body, and may mean you should stop taking the drug), urticaria, severe allergic reaction, joint pains, muscle pains, sensitivity to light; dry mouth, nervousness, anxiety, headaches, sleep problems, shaking, dizziness, loss of energy, hallucinations, drowsiness, fits, production of breast milk, sexual problems, difficulty urinating, sweating, movement disorders, sight problems, low blood sodium, and bleeding disorders; suicidal thoughts; very rarely, angle closure glaucoma. The most commonly reported sexual difficulties in men are reduced sexual desire, prolonged erection, failed erection, delayed ejaculation and lack of orgasm. In women, the effects are more varied and may include spontaneous orgasm, delayed or lack

of orgasm (associated with the drug fluoxetine) or increased libido (with fluvoxamine). Such problems may be treatable by lowering the dose, changing to an alternative drug or stopping the drug for a while, but in some people these effects may persist after the drug has been withdrawn. (Because of these side effects, these drugs are sometimes used to treat sexual difficulties, such as premature ejaculation).

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.

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 mental restlessness and agitation that causes great unease, and is more commonly associated with antipsychotic medication. Anyone who experiences such a sensation while taking an SSRI should discuss this with their 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. All currently available SSRIs (except, perhaps, citalopram) 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. If SSRIs are given with other antidepressants including MAOIs, tryptophan and lithium, there is a risk of serotonin syndrome developing. This is serious and potentially fatal. The symptoms are: hyperthermia (high temperature), tremor and convulsions (fits), agitation and muscle spasms.

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.

Adult dose: 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. 31; in addition: palpitations, fast heart beat, low blood pressure on standing, coughing, yawning, confusion, difficulty concentrating, feeling unwell, memory problems, migraine, tingling feelings, abnormal dreams, taste disturbance, increased saliva, stuffy nose, ringing in the ears, problems with urinating, 'high' mood, anxiety. **Caution:** see general SSRIs on p. 31. **Drug interactions:** may have fewer interactions with other drugs than other SSRIs.

Escitalopram (Cipralext)

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.

Adult dose: 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. 31; in addition: sinusitis, yawning; fatigue, restlessness, abnormal dreams, tingling; high temperature; less commonly taste disturbance, tooth grinding, fainting, fast heart beat, oedema (puffiness), confusion, disturbances of menstrual periods, nose bleeds, dilation of pupils, ringing in the ears, itching, and hair loss; rarely slow heart beat, aggression, and depersonalisation (feeling detached from your surroundings); liver disease, low blood pressure on standing, affects on heart rhythm and blood problems also reported; increased anxiety during initial treatment of panic disorder (reduce dose). **Caution:** see general SSRIs on p. 31. **Drug interactions:** see citalopram.

Fluoxetine (Oxactin, Prozac)

Form: capsules or liquid.

Adult dose: 20mg daily for depression should be enough. 60mg daily if given for the eating problem bulimia nervosa. 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. 31; also dilatation of blood vessels, low blood pressure on standing, sore throat, breathing problems, chills, taste disturbances, sleep disturbances, feelings of excitement, confusion, yawning, difficulty concentrating, changes in blood sugar, hair loss, increased urinary frequency; rarely lung disease; very rarely liver disease, serious skin problems, and a condition similar to neuroleptic malignant syndrome (see *Making sense of antipsychotics*) **Drug interactions:** MAOIs should not be given until at least five weeks after stopping fluoxetine.

Fluvoxamine (Faverin)

Form: tablets.

Adult dose: 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 and cautions:** 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 *Making sense of antipsychotics*), abnormal liver function – treatment should be discontinued. **Drug interactions:** see fluoxetine, and general SSRIs on p. 31. 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.

Adult dose: 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 and cautions:** see general SSRIs on p. 31; also yawning; 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 *Making sense of antipsychotics*), very rarely puffy hands and feet, acute glaucoma, liver disorders (e.g. hepatitis), and

spontaneous erection without sexual desire (priapism: medical advice should be sought).

The Commission on Human Medicines has received more reports of neuromuscular reactions (involuntary movements of mouth and face) for paroxetine than for other SSRIs. A 1993 Drug Safety Research Unit report revealed a higher rate of male sexual dysfunction than with other SSRIs. **Drug interactions:** see general SSRIs on p. 31. MAOIs should not be used within two weeks of stopping paroxetine.

Sertraline (Lustral)

Form: tablets.

Adult dose: 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 and cautions:** see general SSRIs on p. 31, but sertraline has been shown to be safe for people with unstable angina or who have had a recent heart attack. Also pancreatitis, hepatitis, jaundice, liver failure, fast heart rate, low blood pressure on standing, memory problems, tingling, aggression, urinary incontinence, and menstrual irregularities.

Drug interactions: see general SSRIs on p. 31. After stopping sertraline, MAOIs should not be taken within seven days.

SSRI-related antidepressants (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 *Drug and Therapeutics Bulletin* concluded that there is no place for it in the treatment of depression.

Form: capsules.

Adult dose: 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:** nausea, vomiting, indigestion, constipation, diarrhoea, abdominal pain, weight changes, decreased appetite, wind, dry mouth; palpitations, hot flushes; difficulty sleeping, abnormal dreams, tingling, drowsiness, anxiety, headache, dizziness, fatigue, weakness, tremor, nervousness, loss of appetite; sexual problems; sight problems; sweating, itching; less commonly sore stomach, smelly breath, liver problems, tooth grinding, fast heart rate, high blood pressure, low blood pressure on standing, fainting, raised cholesterol, vertigo, taste disturbance,

cold hands and feet, problems with temperature control, difficulty concentrating, movement disorders, muscle twitching, muscle and joint pain, thirst, sore mouth, underactive thyroid, difficulties with urination, and sensitivity to light; rarely mania and angle-closure glaucoma; also reported problems with heart rhythm, chest pain, hallucinations, suicidal behaviour, fits, allergic reactions (including Stevens-Johnson syndrome – a very serious illness) and anaphylaxis, low blood sodium. **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 and Efexor 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.

Adult dose: 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, then gradually reduced. Efexor XL is a modified release form, available as 75mg and 150mg, enabling the daily dose to be taken all at once. Manufacturers suggest new users start on 75mg once daily, increasing after two weeks to 150mg if necessary. Maximum dose 225mg daily. Best taken at the same time each day. **Side effects:** constipation, nausea, anorexia, weight changes, diarrhoea, indigestion, vomiting, abdominal pain; high blood pressure, palpitation, dilatation of blood vessels, changes in cholesterol levels; chills, high temperature, breathing problems, yawning; dizziness, dry mouth, insomnia, nervousness, drowsiness, loss of energy, headache, abnormal dreams, agitation, anxiety, confusion, increased muscle tension, tingling, shaking; urinary frequency, sexual problems, menstrual disturbances; joint pain, muscle pain; sight problems, dilatation of pupil of eye (very rarely angle-closure glaucoma); ringing in the ears; sweating, itch, rash; less commonly tooth grinding, taste disturbance, low blood pressure and low blood pressure when standing, disturbances of heart rhythm, syndrome of inappropriate anti-diuretic hormone secretion, apathy, hallucinations, muscle spasms, urinary retention, bleeding disorders, hair loss, allergic reactions including swelling of skin, itchy rash, sensitivity to light; rarely liver disease, unsteadiness, loss of co-ordination, speech disorder, mania and hypomania, fits, and neuroleptic malignant syndrome, Stevens-Johnson syndrome (a very serious allergic illness); very rarely pancreatitis, disturbances of heart rhythm, aggression, delirium, movement disorders including severe restlessness, raised levels of the hormone prolactin, blood diseases, muscle break-down; suicidal behaviour. Driving and other skilled tasks may be affected.

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. **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, light-headedness, 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.

Noradrenaline reuptake inhibitor (NARI)

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.

Form: tablets.

Adult dose: 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:** nausea, dry mouth, constipation, loss of appetite; fast heart rate, palpitation, dilatation of blood vessels, low blood pressure when standing; headache, lack of sleep, dizziness; chills; impotence; urinary retention; sight problems; sweating; lowering of blood in older people; very rarely angle-closure glaucoma; also reported vomiting, high blood pressure, tingling, agitation, anxiety, irritability, hallucinations, aggression, cold hands and feet, and rash; suicidal behaviour. **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.

Combination or compound drugs

Sometimes drugs are made which combine two or more medicines into one tablet. However, the BNF does not recommend this, mainly because the doses of each separate drug can't be adjusted to individual needs. It may be preferable to prescribe the two kinds of drugs separately. People who have been taking a combination drug for more than a few months should ask their doctor to take a fresh look at their needs. The drug Triptafen combines an antidepressant with an antipsychotic in these proportions:

Triptafen: 25mg amitriptyline hydrochloride; 2mg perphenazine.

Triptafen-M: 10mg amitriptyline hydrochloride; 2mg perphenazine.

The dose of perphenazine is low and considered unlikely to cause the severe side effects associated with antipsychotic drugs. People who experience muscle spasms, or tics or effects which mimic Parkinson's disease while taking Triptafen should talk to their doctor. For more information about perphenazine, see *Making sense of antipsychotics*.

Other drugs for treating depression

Flupentixol/flupenthixol (Fluanxol)

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.

Adult dose: 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.

Lithium (Camcolit, Liskonum, Priadel)

Lithium is mainly used for bipolar disorder, but may also be given as a preventive therapy where there are repeated episodes of severe depression. (See *Making sense of lithium* for more information.)

Tryptophan/L-tryptophan (Optimax)

Tryptophan is an amino acid present in the normal diet in small quantities. It has been used as an antidepressant since the 1970s, but the then Committee on Safety of Medicines withdrew it from general use in 1990 because it was associated with a serious illness eosinophilia-myalgia syndrome (EMS). This is a blood disorder bringing severe muscle pain, joint pain, fever, swelling and skin rash, which may involve the lungs and central nervous system. The company warns that EMS is 'a multi-system disorder, which is usually reversible, but rarely fatal'. It states that various investigations have not as yet precisely identified the cause, which may have been associated with a contaminated batch of the drug. Tryptophan was re-introduced in 1994 for 'exceptional cases' of treatment-resistant depression. It can only be prescribed by hospital specialists for people 'who have had severe and disabling depression continuously for more than two years'. Both patient and prescribing doctor must be registered with the manufacturer. The manufacturer recommends blood monitoring (for eosinophil count, a particular white blood cell) and monitoring for any muscular symptoms. Safety questionnaires are issued to the prescriber every three months to begin with, and thereafter six-monthly. The Commission on Human Medicines reviews the information.

Form: tablets. **Adult dose:** 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:** drowsiness, nausea, headache, light-headedness, suicidal behaviour. **Drug interactions:** the BNF warns that prescribing Optimax with other antidepressants may be hazardous. They specify MAOIs and SSRIs, yet also indicate it should only be used as an adjunct to other antidepressant medication.

Caution: drug manufacturers point out that it is only available under the limited circumstances previously mentioned, and from hospital specialists. It should not be given to people who have had EMS following tryptophan use. Manufacturers advise against using it in pregnancy or while breastfeeding.

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Useful organisations

Mind

Mind is the leading mental health organisation in England and Wales, providing a unique range of services through its local associations, to enable people with experience of mental distress to have a better quality of life. For more information about any mental health issues, including details of your nearest local Mind association, contact the Mind website: www.mind.org.uk or Mind*info*Line on 0845 766 0163.

British Association for Behavioural and Cognitive Psychotherapies (BABCP)

tel. 0161 797 4484 web: www.babcp.com
Can provide details of accredited therapists

British Association for Counselling and Psychotherapy (BACP)

tel. 01455 883 300 (general enquiries)
tel: 0870 443 5220 (to find a therapist)
web: www.bacp.co.uk
For details of local practitioners

Carers UK

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

MDF The Bipolar Organisation

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

Medicines and Healthcare products Regulatory Agency (MHRA) (and Commission on Human Medicines)

tel. 020 7084 2000 web: www.mhra.gov.uk
See their website for documents on taking medicines

UK Council for Psychotherapy (UKCP)

tel. 020 7014 9955 web: www.psychotherapy.org.uk

Maintains a voluntary register of qualified psychotherapists

Yellow Card Scheme

hotline: 0808 100 3352 (business hours)

web: www.yellowcard.gov.uk

For reporting side effects and withdrawal effects of drugs. Also has a translation service for those whose first language is not English

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

www.medicines.org.uk

For detailed information on drugs, including the half-lives of individual drugs

Further reading and order form

- The BMA new guide to medicines and drugs (seventh edition)* The British Medical Association (Dorling Kindersley, 2004) £16.99
- Coming off antidepressants* J. Glenmullen (Robinson, 2006) £9.99
- Coming off psychiatric drugs: successful withdrawal from neuroleptics, antidepressants, lithium, carbamazepine and tranquillisers* P. Lehmann (ed) (Peter Lehmann Publishing, 2004) £14.99
- Coping with coming off* (Mind report 2005) £5
- Drugs used in the treatment of mental health disorders: FAQs* (fourth edition) S. Bazire (Academic Publishing Services 2004) £9.95
- How to cope with sleep problems* (Mind 2005) £1
- Inside out (a guide to the self-management of manic depression)* (Manic Depression Fellowship 1995) £3
- Making sense of antipsychotics* (major tranquillisers) (Mind 2007) £2.50
- Making sense of cognitive behaviour therapy* (Mind 2007) £2.50
- Making sense of coming off psychiatric drugs* (Mind 2005) £2.50
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- The Mind guide to food and mood* (Mind 2006) £1
- The Mind guide to managing stress* (Mind 2006) £1
- Mind rights guide 3: consent to medical treatment* (Mind 2008) £1
- Understanding anxiety* (Mind 2008) £1
- Understanding depression* (Mind 2007) £1
- Understanding bipolar disorder* (manic depression) (Mind 2006) £1
- Understanding mental illness* (Mind 2007) £1
- Understanding obsessive-compulsive disorder* (Mind 2008) £1
- Understanding postnatal depression* (Mind 2008) £1
- Understanding self-harm* (Mind 2007) £1
- Understanding talking treatments* (Mind 2005) £1
- Your drug may be your problem: how and why to stop taking psychiatric medications* P. Breggin, D. Cohen (Da Capo Press 2007) £9.99

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- We provide information and support, campaign to improve policy and attitudes and, in partnership with independent local Mind associations, develop local services.
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