

PACKAGE LEAFLET: Information for the patient

AMIPTYL

Film-coated tablets – 25 mg

(Amitriptyline hydrochloride)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Amiptyl is and what it is used for
2. Before you take Amiptyl
3. How to take Amiptyl
4. Possible side effects
5. How to store Amiptyl
6. Other information

1. WHAT AMIPTYL IS AND WHAT IT IS USED FOR

Amiptyl is a tricyclic antidepressant that has a structure with three rings. It inhibits the neuronal reuptake of noradrenaline and of serotonin (5-HT) in the central nervous system. The inhibition of these monoamino-neurotransmitters, which potentiate the action of amitriptyline in the brain, seems to be related with its antidepressant activity. If the sedative effect and other side effects of amitriptyline are observed at the beginning of the treatment, the antidepressant effect is noticed only after some weeks.

Amiptyl film-coated tablets are used for:

- Depression in adults (major depressive episodes);
- Neuropathic pain in adults;
- Prevention of chronic tension-type headaches in adults;
- Prevention of migraine in adults;
- Bed-wetting at night (Nocturnal enuresis) in children aged 6 years and above, only when organic causes, such as spina bifida and related disorders, have been excluded and no response has been achieved to all other non-drug and drug treatments, including muscle relaxants and desmopressin; Amiptyl should only be prescribed by doctors with expertise in treating patients with persistent bed-wetting.

2. BEFORE YOU TAKE AMIPTYL

Do not take Amiptyl if:

- you suffer from hypersensitivity to amitriptyline, to the other tricyclic antidepressants, or to any of the other excipients of Amiptyl film-coated tablets listed in section 6;
- you have recently had a heart attack;
- you have heart problems such as disturbances in heart rhythm which are seen on an electrocardiogram (ECG), heart block, or coronary artery disease;
- you concomitantly take monoamine oxidase (MAO) inhibitors;
- you have taken an MAO inhibitor in the last 14 days;
- you have taken moclobemide (an MAO inhibitor) the day before;
- you suffer from severe liver diseases.

If you are being treated with Amiptyl, you must stop taking this medicine and then wait for 14 days before you start treatment with an MAO inhibitor.

In these cases consult with your doctor or go directly to the hospital.

This medicine must not be used in children under 6 years of age.

Take special care with Amiptyl

Consult with your doctor or pharmacist before taking Amiptyl.

The use of buprenorphine / opioids together with Amiptyl can lead to serotonin syndrome, a potentially life-threatening condition (see section “Taking other medicines”).

Heart rhythm disorders and hypotension may occur if you receive a high dosage of amitriptyline. This might also occur in usual doses if you have had a heart condition before.

Prolonged QT interval

A heart problem called “prolonged QT interval” (which is shown on your electrocardiogram, ECG) and heart rhythm disorders (rapid or irregular heart beat) have been reported with Amiptyl.

Tell your doctor if you:

- have slow heart rate;
- have or had a problem where your heart cannot pump the blood round your body as well as it should (a condition called heart failure);
- are taking any other medicines that may cause heart problems, or
- you have a low level of potassium or magnesium, or a high level of potassium in your blood;
- have a surgery planned as it might be necessary to stop the treatment with amitriptyline before you are given anaesthetics; in the case of acute surgery, the anaesthetist should be informed about the treatment of amitriptyline;
- have an over active thyroid gland or are taking thyroid medication.

Thoughts of suicide and worsening of your depression or anxiety disorder

If you are depressed, you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer.

You may be more likely to think like this:

- if you have previously had thoughts about killing or harming yourself.
- if you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in young adults (less than 25 years old) with psychiatric conditions who

were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed, and ask them to read this leaflet. You might ask them to tell you if they think your depression or anxiety is getting worse, or if they are worried about changes in your behaviour.

Episodes of mania

Some patients with manic-depressive illness may enter into a manic phase. This is characterized by profuse and rapidly changing ideas, exaggerated gaiety and excessive physical activity. In such cases, it is important to contact your doctor who probably will change your medication.

Tell your doctor if you, or have had in the past, any medical problems, especially if you have:

- narrow angle glaucoma (loss of vision due to abnormally high pressure in the eye);
- epilepsy, a history of convulsions or fits;
- difficulty in passing urine;
- enlarged prostate;
- thyroid disease;
- bipolar disorder;
- schizophrenia;
- severe liver disease;
- severe heart disease;
- pylorus stenosis (narrowing of the gastric outlet) and paralytic ileus (blocked intestine);
- diabetes as you might need an adjustment of your antidiabetic medicine.

If you use antidepressants such as SSRIs, your doctor might consider changing the dose of your medicine.

Elderly are more likely to suffer from certain side effects, such as dizziness when you stand up due to low blood pressure (see also section “Possible side effects”).

Children and adolescents

Depression, neuropathic pain, prevention of chronic tension-type headaches and migraines

Children and adolescents aged below 18 years must not take Amiptyl for these indications as safety and efficacy have not been established in this age group.

Bed-wetting at night (Nocturnal enuresis)

- An ECG should be performed prior to initiating therapy with amitriptyline to exclude long QT syndrome;
- This medicines should not be taking at the same time as an anticholinergic drug (see also section “Taking other medicines”);
- Suicidal thoughts and behaviours may also develop during early treatment with antidepressants for disorders other than depression; the same precautions observed when treating patients with depression should therefore be followed when treating patients with bed-wetting.

Taking other medicines

Some medicines may affect the action of other medicines and this can sometimes cause serious side effects.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines such as:

- monoamine oxidase inhibitors (MAOIs) e.g. phenelzine, iproniazid, isocarboxazid, nialamide or tranylcypromine (used to treat depression) or selegiline (used to treat Parkinson's disease); these should not be taken at the same time as Amiptyl (see section “Do not take Amiptyl”);
- adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine (these may be present in cough or cold medicine, and in some anaesthetics);
- medicines to treat high blood pressure for example calcium-channel blockers (e.g. diltiazem and verapamil), guanethidine, betanidine, clonidine reserpine and methyldopa;
- anticholinergic drugs such as certain medicines to treat Parkinsons disease and gastrointestinal disorders (e.g. atropine, hyoscyamine);
- thioridazine (used to treat schizophrenia);
- tramadol (painkiller);

- medicines to treat fungal infections (e.g. fluconazole, terbinafine, ketoconazole, and itraconazole);
- sedatives (e.g. barbiturates);
- antidepressants (e.g SSRIs (fluoxetine, paroxetine, fluvoxamine), duloxetine and bupropion);
- buprenorphine / opioids may interact with Amiptyl and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, hallucinations, coma, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C; contact your doctor when experiencing such symptoms;
- medicines for certain heart conditions (e.g. beta blockers and antiarrhythmics);
- cimetidine (used to treat stomach ulcers);
- methylphenidate (used to treat ADHD);
- ritonavir (used to treat HIV);
- oral contraceptives;
- rifampicin (to treat infections);
- phenytoin and carbamazepine (used to treat epilepsy);
- St. John's Wort (hypericum perforatum) – an herbal medicine used for depression;
- thyroid medication;
- valproic acid.

You should also tell your doctor if you take or have recently taken medicine that may affect the heart's rhythm. e.g.:

- medicines to treat irregular heartbeats (e.g. quinidine and sotalol);
- astemizole and terfenadine (used to treat allergies and hayfever);
- medicines used to treat some mental illnesses (e.g. pimozide and sertindole);
- cisapride (used to treat certain types of indigestion);
- halofantrine (used to treat malaria);
- methadone (used to treat pain and for detoxification);
- diuretics ("water tablets" e.g. furosemide).

If you are going to have an operation and receive general or local anaesthetics, you should tell

your doctor that you are taking Amiptyl.

Likewise, you should tell your dentist that you take Amiptyl if you are to receive a local anaesthetic.

Taking Amiptyl with food and drinks

It is advised not to take Amiptyl with alcoholic drinks.

Pregnancy and breastfeeding

Ask for the advice of your doctor or pharmacist before taking this drug.

Amiptyl is not recommended during pregnancy unless your doctor considers it clearly necessary, and only after a careful risk/benefit assessment.

If you have taken this medicine during the last part of the pregnancy, the newborn may have withdrawal symptoms such as irritability, increased muscle tension, tremor, irregular breathing, poor drinking, loud crying, urinary retention (withholding/retaining urine), and constipation.

Your doctor will advise you whether to start / continue / stop breastfeeding, or stop using this medicine taking into account the benefit of breast-feeding for your child and the benefit of therapy for you.

Driving and using machinery

Amiptyl may cause drowsiness and dizziness, especially at the beginning of the treatment. For this reason, patients who are being treated with Amiptyl, should not drive or use machines.

Important information about some of the excipients of Amiptyl

Amiptyl contains lactose. If you have an intolerance to some sugars, contact your doctor before taking this drug.

Amiptyl contains the azodyes Sunset yellow FCF (E 110) and Ponceau 4R (E 124), which may cause allergic reactions.

3. HOW TO TAKE AMIPTYL

Always take Amiptyl as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. Not all dosage schemes can be achieved with all the pharmaceutical forms/strengths. The appropriate form/strength should be selected for the initial dosage and for all subsequent dosage increases.

Amiptyl can be taken with or without food. The tablets are swallowed with a glass of water. Do not chew the tablets.

Depression

Adults

The recommended starting dose is 25 mg twice a day. Depending on your response to the medicine, your doctor may gradually increase the dose up to 150 mg per day (in two partial doses).

Elderly patients over 65 years of age and patients with cardiovascular disease

The recommended starting dose is 10 mg - 25 mg daily.

Depending on your response to the medicine, your doctor may gradually increase the dose up to a total daily dose of 100 mg divided into two doses. If you receive a daily dose between 100 and 150 mg, your doctor may check you more often.

Use in children and adolescents

This medicine should not be used to treat depression in children and adolescents. For more information, see section 2.

Neuropathic pain, prevention of chronic tension-type headaches and migraines

Your doctor will adjust your treatment with Amiptyl according to your symptoms and how you respond to the treatment.

Adults

The recommended starting dose is 10 mg - 25 mg in the evening.

Recommended daily doses are 25 mg - 75 mg.

Depending on your response to the medicine, your doctor may gradually increase the dose. If you receive a dose of more than 100 mg a day, your doctor may check you more often. Your doctor will tell you whether you should take the dose once a day or divided into two doses.

Elderly patients over 65 years of age and patients with cardiovascular disease

The recommended starting dose is 10 mg - 25 mg in the evening.

Depending on your response to the medicine, your doctor may gradually increase the dose. If you receive a daily dose above 75 mg, your doctor may check you more often.

Use in children and adolescents

This medicine should not be used in children and adolescents for the treatment of neuropathic pain or for the prevention of chronic tension headache or migraine. For more information, see section 2.

Bed-wetting at night (Nocturnal enuresis)

Use in children and adolescents

The recommended dosages for children are:

- under 6 years: see section 2 under "Amiptyl must not be taken".
- from 6 to 10 years: 10 mg - 20 mg daily. A suitable dosage form should be used for this age group.
- from 11 years: 25 mg - 50 mg.

The dose should be increased gradually.

Take this medicine 1 - 1½ hours before going to bed. Before starting treatment, your doctor will do an ECG to check your heart activity for signs of irregular heartbeat.

After 3 months, your doctor will review the treatment and then do another ECG if needed.

Do not stop the treatment without consulting your doctor.

Patients with special risks

Patients with liver disease and those who metabolise more slowly are usually treated with a lower dose.

The doctor may take blood samples to find out how high the concentration of amitriptyline is in your blood (see also section 2).

Duration of the treatment

Do not change the dose of the medicine or stop taking it without first talking to your doctor.

Depression

As with other medicines used to treat depression, it may take a few weeks before you notice any improvement.

The duration of treatment for depression depends on the individual case; as a rule it is at least 6 months. Your doctor decides on the duration of treatment.

Continue to take this medicine for as long as your doctor advises.

The underlying disease may persist for a long time. If you stop the treatment too early, the symptoms may return.

Neuropathic pain, prevention of chronic tension headaches and migraines

It may take several weeks for your pain to improve.

Talk to your doctor about the duration of treatment and continue to take this medicine for as long as your doctor advises.

Bed-wetting at night (Nocturnal enuresis)

The doctor will check after 3 months whether the treatment should be continued.

If you take more Amiptyl

Contact your doctor or go to the nearest hospital immediately. Do this even if there are no signs of discomfort or poisoning. Take this medicine with you if you go to the hospital.

Symptoms of overdose include:

- dilated pupils;

- fast or irregular heartbeats;
- difficulties urinating;
- dry mouth and tongue;
- constipation;
- fits;
- fever;
- agitation;
- confusion;
- hallucinations;
- uncontrolled movements;
- low blood pressure, weak pulse, pallor;
- difficulty breathing;
- discolouration of the skin;
- decreased heart rate;
- drowsiness;
- loss of consciousness;
- coma;
- various cardiac symptoms such as heart block (abnormal heart rhythm due to issue with the heart's electrical system), heart failure (failure in the functioning of the heart), hypotension (decrease in blood pressure), cardiogenic shock (a condition in which your heart suddenly can't pump enough blood to meet your body's needs), metabolic acidosis (a condition that occurs when the body produces excessive quantities of acid), hypokalemia (decrease in the potassium level in the blood).

Overdose with amitriptyline in children could have serious consequences. Children are especially susceptible to coma, cardiac symptoms, difficulty in breathing, seizures, low blood sodium level, lethargy, drowsiness, nausea, vomiting and high blood sugar level.

If you forget to take Amiptyl

If you forget a dose (or more doses), take the next dose when it is time to take it usually.

Do not take a double dose (or higher) to make up for a forgotten dose (doses).

If you stop taking Amiptyl

Amiptyl should be gradually withdrawn to avoid the risk of relapse. Your doctor will decide when and how to stop your treatment to avoid any unpleasant symptoms that might occur if it is stopped abruptly (e.g. headache, feeling unwell, sleeplessness and irritability).

If you have further questions on the use of this medicinal product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all other medicines, Amiptyl may cause side effects, although not everybody manifests them.

If you get any of the following symptoms you should see your doctor immediately:

- **Common:** A heart problem called “prolonged QT interval” (that appears on your electrocardiogram, ECG).
- **Rare:**
 - Severe constipation, a swollen abdomen, fever and vomiting; these symptoms may be due to parts of the intestine becoming paralysed.
 - Any yellowing of the skin and the white in the eyes (jaundice); your liver may be affected.
 - Bruising, bleeding, pallor or persistent sore throat and fever; these symptoms can be the first signs that your blood or bone marrow may be affected; effects on the blood could be a decrease in the number of red cells (which carry oxygen around the body), white cells (which help to fight infection) and platelets (which help with clotting).
 - Suicidal thoughts or behaviour.
- **Very rare:** Attacks of intermittent blurring of vision, rainbow vision, and eye pain; you should immediately have an eye examination before the treatment with this medicine can be continued; this condition may be signs of acute glaucoma.

Side effects listed below have been reported in the following frequencies:

Very common (may affect more than 1 in 10 people):

- sleepiness/drowsiness;
- shakiness of hands or other body parts;
- dizziness;

- headache;
- irregular, hard, or rapid heartbeat;
- dizziness when you stand up due to low blood pressure (orthostatic hypotension);
- dry mouth;
- constipation;
- nausea;
- excessive sweating;
- weight gain;
- slurred or slow speech;
- aggression;
- problem with ability of the eye to change its focus from distant to near objects (and vice versa);
- congested nose.

Common (may affect up to 1 in 10 people):

- confusion;
- sexual disturbances (decreased sex-drive, problems with erection);
- Attention Deficit Disorder;
- changes in taste;
- numbness or tingling in the arms or legs;
- disturbed coordination;
- dilated pupils;
- heart block;
- fatigue;
- low sodium concentration in the blood;
- restlessness;
- urination disorders;
- feeling thirsty.

Uncommon (may affect up to 1 in 100 people):

- agitation, anxiety, difficulties sleeping, nightmares;

- cramps;
- ringing in the ears (tinnitus);
- high blood pressure;
- diarrhoea, vomiting;
- skin rash, hives (urticaria), swelling of the face and tongue;
- difficulties urinating;
- increased production of breast milk or breast milk outflow without breast feeding;
- increased pressure in the eye ball;
- collapse conditions;
- worsening of cardiac failure;
- liver function impairment.

Rare (may affect up to 1 in 1000 people):

- decreased appetite;
- delirium (especially in elderly patients), hallucinations;
- abnormality in the heart's rhythm, or heartbeat pattern;
- swelling of the salivary glands;
- hair loss;
- increased sensitivity to light;
- breast enlargement in men;
- fever;
- weight loss;
- abnormal results of liver function tests.

Very rare (may affect up to 1 in 10,000 people):

- heart muscle disease;
- feeling of inner restlessness and a compelling need to be in constant motion;
- disorder of the peripheral nerves;
- acute increase of pressure in the eyeball (acute glaucoma);
- particular forms of abnormal heart rhythm (so called torsades de pointes);
- allergic inflammation of the lung alveoli and of the lung tissue.

Not known (frequency cannot be estimated from available data):

- loss of appetite;
- elevation or lowering of blood sugar levels;
- paranoia;
- movement disorders (involuntary movements or decreased movements);
- hypersensitivity inflammation of heart muscle;
- hepatitis (inflammation of the liver) with signs such as dark urine, weight loss and jaundice;
- hot flush;
- dry eyes.

An increased risk of bone fractures has been observed in patients taking this type of medicines.

If any of the side effects worsen, or if you notice side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. HOW TO STORE AMIPTYL

Keep out of the reach and sight of children!

Do not use Amiptyl after the expiry date which is stated on the package.

Store below 25°C!

Store in the original packaging to protect it from light.

6. OTHER INFORMATION

What Amiptyl film-coated tablets contain

The active substance is amitriptyline hydrochloride.

One film-coated tablet contains 25 mg amitriptyline hydrochloride.

The excipients are:

Tablet core: microcrystalline cellulose, lactose monohydrate, purified talc, magnesium stearate;

Film-coating: polyvinyl alcohol, macrogol, titanium dioxide, Ponceau 4R (E124), Sunset yellow FCF (E110), Brilliant blue FCF.

Content of the pack

Carton box with 30 film-coated tablets.

Marketing Authorisation Holder (MAH) and Manufacturer

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