Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Elatrol

Tablets

Composition

Each tablet contains:

Amitriptyline Hydrochloride 25 mg

Elatrolet

Tablets

Composition

Each tablet contains:

Amitriptyline Hydrochloride 10 mg

For information about inactive ingredients and allergens, see section 2 under 'Important information about some of this medicine's ingredients' and section 6 - 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Medical activity

For the treatment of symptoms of depression and treatment of bed-wetting at night (enuresis nocturna).

Therapeutic group

Non-selective monoamine reuptake inhibitors (N06AA).

2. Before using this medicine

Do not use this medicine if:

- you are sensitive to the active ingredient or to any of the other ingredients in this medicine (see section 6 - 'Additional information')
- you have recently had a heart attack (myocardial infarction)
- you have any heart problems such as: disturbances in heart rhythm which are seen on an electrocardiogram (ECG), heart block, or coronary artery disease
- you are taking monoamine oxidase inhibitors (MAOIs)
- you have taken MAOIs within the last 14 days
- you have taken moclobemide the day before

- you have severe liver disease
- you are treated with Elatrol/Elatrolet tablets, you have to stop taking this medicine and wait for 14 days before starting treatment with a MAOI.
- you are below 12 years of age.

Special warnings about using this medicine:
Tell your doctor or pharmacist before starting treatment with Elatrol/Elatrolet tablets.
Heart rhythm disorders and hypotension may occur if you receive a high dosage of the medicine. These effects might also occur in usual doses if you have pre-existing heart disease.

Prolonged QT interval
A heart problem called prolonged QT interval (which can be seen on your electrocardiogram, ECG) and heart rhythm disorders (rapid or irregular heartbeat) have been reported in treatment with Amitriptyline.
Tell your doctor if:

- you have a slow heart rate
- you have or had a problem where your heart cannot pump the blood around your body properly (a condition called heart failure).
- you are taking any other medication that may cause heart problems, or
- you have a problem that gives you a low level of potassium or magnesium, or a high level of potassium in your blood.
- you have a surgery planned, it might be necessary to stop the treatment with Amitriptyline before you are given an anaesthetic. In the case of acute surgery, the anaesthetist should be informed that you are taking Amitriptyline.
- you have an overactive thyroid gland or take medications to treat a thyroid function disorder.

Thoughts of suicide, worsening of your depression or anxiety
If you suffer from depression, you may sometimes have thoughts of killing or harming yourself. These may be increased when first starting antidepressants, since it takes time for these medicines 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
- you are a young adult. Information from clinical studies has shown an increased risk of suicidal behaviour in adults (less than 25 years old) with psychiatric conditions who were treated with an antidepressant.

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

It may be 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 disorder 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 have, 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 a blocked intestine (paralytic ileus)
- diabetes (you might need an adjustment of the dosage of your antidiabetic medicines)

If you use antidepressants such as SSRIs, your doctor might consider changing the dosage of your medicine (see section 2 – 'Drug interactions')

The use of buprenorphine together with amitriptyline can lead to serotonin syndrome (which may be a life-threatening condition), see section 2 – 'Drug interactions'

Elderly are more likely to suffer from certain side effects such as dizziness when standing up due to low blood pressure (see section 4, 'Side effects')

Use in children and adolescents

- *Depression*
  Do not give this medicine to children and adolescents aged below 18 years for treatment of depression as long-term safety and efficacy have not been established in this age group.

- *Bed-wetting at night*
  - ECG should be performed prior to initiating therapy this medicine to exclude long QT syndrome.
  - This medicine should not be taken at the same time as an anticholinergic drug (see section 2 - 'Drug interactions')

Suicidal thoughts and behaviours may also appear in early stages of treatment with antidepressants for disorders other than depression; therefore, in patients with

enuresis, the same precautions observed when treating patients with depression should be followed.

Drug interactions:
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- MAOIs (e.g. phenelzine, iproniazid, isocarboxazid, nialamide or tranylcypromine (for treatment of depression)) or selegiline (for treatment of Parkinson's disease). These medicines should not be taken at the same time as Amitriptyline (see section 2 - 'Do not use this medicine if')
- adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine (these may be present in cough or cold medicine, and in some anaesthetics)
- medicine to lower high blood pressure for example calcium-channel blockers (e.g. diltiazem and verapamil), guanethidine, betanidine, clonidine reserpine and methyldopa
- Anticholinergic medicines such as certain medicines to treat Parkinson's 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)
- medicines for certain heart conditions (e.g. beta blockers, antiarrhythmics)
- cimetidine (used to treat stomach ulcers)
- methylphenidate (used to treat attention deficit hyperactivity disorder - ADHD)
- ritonavir (used to treat HIV)
- Oral contraceptives
- rifampicin (to treat infections)
- phenytoin and carbamazepine (used to treat epilepsy)
- St. John´s Wort (hypericum – a herbal remedy used for depression)
- thyroid medicines
- valproic acid
- buprenorphine/opioids - These medicines may interact with Amitriptyline and may cause symptoms such as involuntary contractions of muscles, including the muscles that control movement of the eyes, agitation, hallucinations, coma, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C. Contact your doctor if you feel any of these symptoms.

You should also tell your doctor if you take or have recently taken medicines that 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 need to have an operation and receive general or local anaesthetics, you should tell your doctor that you are taking this medicine.

Likewise, you should tell your dentist that you take this medicine if the treatment involves administration of a local anaesthetic.

Using this medicine and food
The medicine can be taken with or without food.

Using this medicine and alcohol consumption
It is not advised to drink alcohol during treatment with this medicine as it might increase the sedative effect.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Taking this medicine is not recommended during pregnancy unless your doctor considers it necessary and only after careful consideration of the benefit versus risk.

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, and constipation.

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

Driving and using machines

Use of this medicine may cause drowsiness and dizziness, especially in the beginning of the treatment. Do not drive or work with machinery if you feel that the medicine affects you in this manner. Children should be cautioned against riding a bicycle, playing near a road, and the like.

Important information about some of this medicine's ingredients
Elatrol and Elatrolet contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, please inform your doctor before taking this medicine.

This medicine contains less than 23 mg of sodium per tablet and is therefore considered ‘sodium free".
Elatrol also contains the colouring agent sunset yellow (E110), which may cause an allergic reaction.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine.

Do not exceed the recommended dose.

Use this medicine at set intervals, as determined by the doctor treating you.

Method of administration
Swallow the medicine with a small amount of water.
Do not split the tablet as there is no score line.
There is no information about crushing or chewing the tablet.

If you have accidentally taken a higher dose
If you have accidentally taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

Symptoms of overdose include:

- dilated pupils,
- fast or irregular heartbeats,
- difficulties passing water,
- dry mouth and tongue,
- intestinal blockage,
- fits,
- fever,
- agitation,
- confusion,
- hallucinations,
- uncontrolled movements,
- low blood pressure, weak pulse, pallor,
- difficulty breathing,
- blue discolouration of the skin,
- decreased heart rate,
- drowsiness,
- loss of consciousness,
- coma,
- various cardiac symptoms such as heart block, heart failure, hypotension, cardiogenic shock, metabolic acidosis, hypokalaemia.

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

If you forget to take the medicine
If you forget to take the medicine at the scheduled time, take a dose as soon as you remember, but under no circumstances should you take both doses together.

Adhere to the treatment as recommended by your doctor.

If you stop taking this medicine
Even if your health improves, do not stop taking this medicine suddenly without consulting your doctor. Your doctor will decide when and how to stop your treatment to avoid any undesired symptoms that might occur if the treatment it is stopped abruptly (e.g. headache, feeling unwell, sleeplessness and irritability).

As with other medicines for the treatment of depression, it may take a few weeks before you feel any improvement.

In treating depression, the duration of treatment is individual, and is usually at least 6 months. The duration of treatment will be determined by your doctor.

Continue to take this medicine for as long as your doctor recommends. The underlying illness may persist for a long time. If you stop your treatment too soon, your symptoms may return.

When treating bed-wetting at night, your doctor will consider if it is necessary to continue treatment after 3 months.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like all medicines, use of Elatrol/Elatrolet may cause side effects, although not everybody gets them. Do not be alarmed by this list of side effects. You may not experience any of them.

Contact your doctor straight away if you have any of the following side effects:

- Attacks of intermittent blurring of vision, rainbow vision, and eye pain. You should immediately have an eye examination before continuing treatment. This condition may indicate acute glaucoma. <u>Rare side effect, may affect up to 1 in 1,000 users.</u>

- A heart problem called prolonged QT interval (which can be seen on your electrocardiogram, ECG). Common side effect, may affect up to 1 in 10 users.
- Bad constipation, a swollen stomach, fever and vomiting. These symptoms may appear due to the intestine becoming paralysed. Rare side effect, may affect up to 1 in 1,000 users.
- Yellowing of the skin and the white in the eyes (jaundice). Your liver may be affected. Rare side effect, may affect up to 1 in 1,000 users.
- Bruising, bleeding, pallor or persistent sore throat and fever. These symptoms can be the first sign of a problem with your blood or bone marrow. 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). Rare side effect, may affect up to 1 in 1,000 users.
- Suicidal thoughts or behaviour. Rare side effect, may affect up to 1 in 1,000 users.

Additional side effects

Very common side effects (appear in more than 1 in 10 users):

- sleepiness/drowsiness
- shakiness of hands or other body parts
- dizziness
- headaches
- 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
- congested nose

Common side effects (appear in up to 1 in 10 users):

- confusion
- sexual disturbances (decreased sex-drive, problems with erection)
- disturbance in attention
- changes in taste
- numbness or a tingling sensation in the arms or legs
- disturbed coordination
- dilated pupils
- heart block
- fatigue
- Low levels of sodium in the blood
- agitation
- urination disorders

- feeling thirsty

Uncommon side effects (appear in up to 1 in 100 users):

- excitement, anxiety, difficulties sleeping, nightmares
- convulsions
- ringing in your ears (tinnitus)
- increased blood pressure
- diarrhoea, vomiting
- skin rash, nettle rash (urticaria), swelling of the face and tongue
- difficulties passing urine
- increased production of breast milk or breast milk outflow without breast feeding
- Increased intraocular pressure
- collapse
- worsening of cardiac failure
- liver function impairment (e.g. cholestasis)

Rare side effects (appear in up to 1 in 1,000 users):

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

Very rare side effects (appear in up to 1 in 10,000 users):

- 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 eye
- certain forms of heart rhythm disorder (so called “torsades de pointes”)
- allergic inflammation of the lung alveoli and of the lung tissue

Side effects of unknown frequency (frequency cannot be estimated from the available data):

- lack of appetite
- elevation or lowering of blood sugar levels
- paranoia
- movement disorders (involuntary movements or decreased movements)
- hypersensitivity inflammation of heart muscle
- hepatitis
- hot flushes

- dry eyes

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

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects:
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:
https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:
Store this medicine in a dry place, below 25ºC.
Do not store different medicines in the same package.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Elatrol:
Lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, colloidal silicon dioxide, hypromellose , titanium dioxide, D&C yellow #10 aluminium lake, macrogol/PEG 400 , FD&C yellow #6/Sunset yellow FCF aluminium lake.

Elatrolet:
Lactose monohydrate, microcrystalline cellulose, starch, sodium starch glycolate, magnesium stearate, colloidal silicon dioxide, hypromellose, titanium dioxide, macrogol/ PEG 400.

What the medicine looks like and contents of the pack:
Elatrolet: White, round biconvex film coated tablets.
Elatrol: Yellow, round biconvex film coated tablets.

Each pack contains 30, 50 or 100 tablets.

Not all pack sizes may be marketed.

Name and address of registration holder and manufacturer:
Teva Israel Ltd.,
124 Dvora HaNevi'a St., Tel Aviv 6944020.

The leaflet was revised in May 2022 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Elatrol: 051.75.24391
Elatrolet: 051.41.24390