Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Anafranil 25 mg
Coated tablets

Each tablet contains:
clomipramine hydrochloride 25 mg

Anafranil SR 75 mg tablets
Slow release tablets

Each tablet contains:
clomipramine hydrochloride 75 mg

Inactive ingredients and allergens in this medicine: 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 for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

Antidepressants increase the risk of suicidal behavior and thoughts in children, adolescents and young adults.

When beginning treatment with this medicine, patients of all ages and their relatives must monitor behavioral changes such as worsening of depression, suicidal thoughts, aggressiveness, etc.

If changes such as these occur, contact your doctor immediately.

1. What is this medicine intended for?

Adults:
Depression of various causes
Obsessive compulsive disorder (OCD)

Children and adolescents (aged 5 to 18 years):
Obsessive compulsive disorder (OCD)

Therapeutic group:
Tricyclic antidepressants, nonselective monoamine reuptake inhibitors.

Anafranil seems to act by increasing the amount of natural chemical transmitters (noradrenaline and serotonin) in the brain by extending the duration of their effect.

2. Before using this medicine
Do not use this medicine:

- If you have hypersensitivity (allergic reaction) to clomipramine or any of the additional ingredients listed in section 6 'Additional information', or any other medicine from the tricyclic antidepressant group
- In combination with medicines from the monoamine-oxidase (MAO) inhibitor group for treatment of depression or during the 21 days after treatment with MAO inhibitors. A 21-day break should be observed between the start of treatment with Anafranil and the discontinuation of treatment with MAO inhibitors
- In combination with antiarrhythmics such as quinidine and propafenone
- If you have recently had a heart attack
- If you suffer from heart rhythm problems (arrhythmias)
- If you have a prolonged QT interval (delay in the activity of the heart which can be seen on ECG)
- If you have glaucoma (increased intraocular pressure)

- If you suffer from acute urinary retention
- If you have severe liver disease

Special warnings about using this medicine
Inform your doctor if you suffer from or have suffered from any of the following disturbances or diseases:
- heart disease
- epilepsy
- difficulty in passing urine (e.g., due to an enlarged prostate)
- increased pressure in the eye (glaucoma)
- overactive thyroid gland or taking thyroid medication at the same time as Anafranil
- tumour of the adrenal gland
- liver or kidney disease
- if you develop dental diseases (e.g., tooth decay)
- if you are planning to have an operation (including minor surgery such as removing a fingernail)
- low blood pressure, because Anafranil can further lower your blood pressure
- constipation. Extreme caution should be exercised when using Anafranil as it can lead to an intestinal obstruction
- heart rhythm disturbances
- suicidal thoughts

Further precautions
- It is important that you and your family or caregivers discuss with your doctor any change in mood during the course of treatment with Anafranil.
- You may experience increased anxiety at the start of treatment with Anafranil (this means that you are responding to the treatment).
- If you wear contact lenses and suffer from eye irritation, inform your doctor, as Anafranil can reduce the flow of tears and cause the mucous membranes to dry out which could damage the cornea.
- Anafranil may cause your skin to be more sensitive to sunlight. Therefore, avoid direct exposure to sunlight, wear sunglasses, and protect your skin with appropriate clothing.
- The doctor must be informed immediately of the appearance of side effects, particularly the occurrence of fever, flu-like symptoms, sore throat or allergic skin reactions, irregular heartbeat, jaundice, itching, swelling of the breasts, spontaneous milk flow, hallucinations, cramps, speech disorders and pregnancy.

Thoughts of killing yourself and worsening of your depression or anxiety and information for families and health care practitioners
In cases of depression or anxiety, you can sometimes have thoughts of killing or harming yourself. The symptoms of depression, particularly suicidal behaviour, may worsen during treatment with Anafranil. When starting to take antidepressants, these types of thoughts may get worse, as the optimal effect of the medicine is not felt immediately. Usually, it takes them some time to work (generally two weeks, but sometimes longer).

Telling a friend or relative that you are depressed or have anxiety can make it easier and be helpful. You may ask the person you share this with to read this leaflet. You could also ask this person to let you know if they think your depression or anxiety has gotten worse,

When Anafranil is given to children and adolescents, pay attention to their behaviour in order to identify suicidal behaviours. If you think of suicide or self-harm or if these thoughts worsen, contact your doctor or go immediately to the nearest hospital.
There have been reports of an increase in the frequency of behavioural disorders - including increased risk of suicidal thoughts, self-harm and suicide - in children, adolescents and young adults (up to the age of 25) with depression or other psychiatric diagnoses, who are being treated with antidepressants. This increase was also observed in patients who had previously had suicidal thoughts or thoughts of self-harm.
These reports were received during clinical trials.

Treatment must not be stopped suddenly, rather only in consultation with the doctor, since withdrawal symptoms may occur (see the Side effects section).
Sudden discontinuation of Anafranil after prolonged treatment can lead to nausea, headaches, vomiting, diarrhoea and anxiety.

If you have been taking another medicine to relieve your symptoms or if you are switching from Anafranil to another medicine, follow your doctor's instructions for taking them. You may need to wait certain time period before taking the other drug (this can be 2-3 weeks).

Smoking
Inform your doctor of changes in smoking habits as smoking significantly lowers the bioavailability of Anafranil.

Children and adolescents
This medicine is not intended for children and adolescents under the age of 18 for the indication of depression of varying origin.
The medicine is not intended for children under the age of 5 for the indication of obsessive-compulsive disorder (OCD).
There is no experience with clomipramine in children under the age of 5 years.

The use of Anafranil to treat depression of varying origins in children and adolescents (0-17 years of age) is not recommended as there is insufficient evidence of the safety and efficacy of Anafranil in the treatment of this indication in children and adolescents.

Elderly patients
Elderly patients generally need lower doses than young and middle-aged patients. Side effects are more likely to occur in elderly patients. The doctor will provide any special information about dosage precautions and the need for close monitoring.

Tests and follow-up
The blood tests ordered by the doctor must be strictly observed.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- antiarrhythmic medicines
- medicines to reduce blood pressure such as alpha-methyldopa, clonidine and guanethidine
- diuretics (combined use may lead to a decrease in blood potassium levels)
- other antidepressants such as selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenergic reuptake inhibitors (SNRIs) and monoamine oxidase inhibitors (MAOIs). Examples of these types of medicine are fluoxetine, fluvoxamine, paroxetine, sertraline, serotonin and tricyclic antidepressants
- sedatives
- epilepsy medicines such as valproic acid
- medicines to prevent blood clots (anticoagulants)
- medicines for asthma or allergies
- medicines for Parkinson’s disease
- thyroid medicines
- medicines with the active ingredient cimetidine that inhibits excessive secretion of gastric acid as the effect of Anafranil may be increased in an undesirable way
- antipsychotic medicines such as thioridazine or chlorpromazine
- sympathomimetic medicines (medicines that mimic substances in the body that stimulate the sympathetic nervous system) such as epinephrine, norepinephrine, isoprenaline, ephedrine and phenylephrine
- hormonal contraceptives (birth control pills)
- rifampicin, an antibiotic used to treat various infections such as tuberculosis
- essence of the Hypericum plant (St. John's wort) is used to relieve depression and anxiety
- buprenorphine, a medicine used to treat addiction to opioids
- terbinafine, used to treat fungal infections of the skin and nails, certain medicines to reduce blood lipids (ion-exchange resin) such as colestipol and cholestyramine

As many medicines may interact with Anafranil, the dose may need to be adjusted or treatment with one of the medicines stopped.

Using this medicine and food
Avoid eating grapefruits and drinking grapefruit juice, cranberry juice.

Alcohol consumption
Avoid drinking alcohol during treatment as Anafranil may reduce alcohol tolerance.

Pregnancy and breast-feeding
Inform your doctor if you are pregnant, planning to become pregnant or are breast-feeding.

Pregnancy
There is limited information on the use of Anafranil in pregnant women that indicates a potential risk of harming the unborn baby or causing congenital birth defects.
Do not take Anafranil during pregnancy, unless specifically prescribed by the doctor.

The doctor will weigh the risk to the unborn baby versus the medical benefit to the mother and make a decision regarding use of Anafranil.

Breast-feeding
The active ingredient of Anafranil passes into breast milk and mothers taking Anafranil are therefore advised not to breast-feed.

Driving and using machines
This medicine may significantly impair your responses, your ability to drive and your ability to use tools or machines
Anafranil may make you sleepy, reduce your alertness, cause blurred vision as well as other nervous system disorders and psychiatric conditions, impair your ability to concentration, cause confusion, worsening of depression, delirium, etc. If this happens to you, avoid driving a vehicle, using machines or any activity that requires full alertness and concentration. These effects may be increased by other medicines or alcohol. Regarding children, they should be cautioned against riding a bicycle or playing near a road, and the like.

Important information about some of this medicine's ingredients
Anafranil 25 mg: The tablet contains lactose and sucrose. If you have been told by your doctor that you have an intolerance to some sugars (e.g., lactose, sucrose), contact your doctor before taking Anafranil 25 mg, coated tablets.

Anafranil SR 75 mg tablets: The tablet contains castor oil which may cause abdominal discomfort and diarrhoea.

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.

Dosage
Only your doctor will determine your dose and how you should take this medicine.
The dosage depends on the age of the patient, the severity, and the type of illness, so it must be adjusted individually in each case.

Adults

Depression of varying origins, obsessive-compulsive disorder
The starting dose is 50-75 mg per day (2-3 Anafranil 25 mg tablets 2-3 times a day or one Anafranil SR 75 mg tablet once a day, preferably in the evening). The doctor can gradually increase the dose during the first week of treatment to 100-150 mg per day (4-6 tablets of 25 mg or 2 tablets of 75 mg).
Your doctor can increase the dosage to a maximum dose of 250 mg per day.
After the symptoms have improved significantly, the doctor can reduce the dosage again to 50-100 mg (2-4 Anafranil 25 mg tablets or 1 Anafranil 75 mg tablet).

The elderly (patients 65 years and older)
Contact your doctor to coordinate alternative treatment.

Children and adolescents (aged 5 to 18 years):
Obsessive-compulsive disorder
Treatment generally starts with 25 mg per day (1 tablet of 25 mg per day). The doctor can increase the dosage in the first two weeks. Since the optimal dose depends on the age and weight of the child, make sure to strictly follow the dosage prescribed by the doctor.

There is no experience with clomipramine in children under the age of 5 years.

The use of Anafranil to treat depression of varying origins in children and adolescents (0-17 years of age) is not recommended as there is insufficient evidence of the safety and efficacy of Anafranil in the treatment of this indication in children and adolescents.

Do not exceed the recommended dose.
Form of administration

The tablet should be swallowed with water.
Anafranil SR 75 mg tablets:
The tablets can be split but should not be chewed.
Anafranil 25 mg: There is no information about splitting or chewing the tablet.

Anafranil can be taken with or without food.

If you have accidentally taken a higher dose
An overdose affects the heart and the nervous system. The following symptoms of overdose usually appear within a few hours: heavy drowsiness; poor concentration; stupor; fast, slow or irregular heartbeat; restlessness and agitation; loss of muscle coordination and muscle stiffness; shortness of breath; seizures; vomiting; fever.
If you have 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. Medical treatment may be necessary.

An overdose of this medicine is particularly dangerous in young children. There are reports of death in children following an overdose.

If you forget to take the medicine
Use this medicine at set intervals, as determined by your doctor.
If you forget to take the medicine at the designated time, take the missed dose as soon as possible and return to the usual dosing schedule. However, if it is almost time to take the next does, skip the missed dose and continue with the regular treatment program. Do not take a double dose.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine
Do not stop taking Anafranil suddenly because this may cause withdrawal symptoms. If your doctor decides to discontinue treatment, they will instruct you on how to lower the dosage gradually to prevent the development of withdrawal symptoms. Gradual reduction is especially important in children and adolescents.

Do not take medicines in the dark! Check the label and the dose every time you take 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

As with any medicine, using Anafranil may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

It is often difficult to distinguish side effects of the medicine from symptoms of depression such as fatigue, sleep disturbances, agitation, anxiety, constipation, and dry mouth.

Elderly patients are particularly sensitive to medicines like Anafranil. Their ability to metabolise and eliminate drugs may be reduced, leading occasionally to reactions going beyond the treatment goals (excessive activity, excessive self-esteem, etc.).

Additional side effects

Very common side effects - effects that appear in more than one in ten users
Increased appetite, weight gain, restlessness, erectile dysfunction (problem with erection) and sex drive (libido), somnolence, dizziness, tremor, headache, muscle twitching, inability to focus vision, blurred vision, dry mouth, constipation, nausea, increased sweating, urination disorders.

Common side effects - effects that appear in 1-10 in 100 users
Confusion, disorientation, hallucinations (particularly in the elderly and patients with Parkinson's disease), anxiety, agitation, sleep disturbances, mania, hypomania (a milder form of mania), aggressiveness, depersonalisation, worsening of depression, sleeplessness, nightmares, acute confusion (delirium), nervosity, poor memory, disturbance in attention, speech disturbances, numbness or a tingling sensation in the arms and legs, taste disturbances, enlarged pupils, ringing in the ears (tinnitus), fast heartbeat, palpitations, hot flushes, low blood pressure and dizziness when changing position, yawning, vomiting, stomach upset, diarrhoea, decreased appetite, allergic reactions such as rash and urticaria, light sensitivity, itchy skin, muscle weakness, muscle stiffness, discharge of milk, enlargement of the breast glands, changes in ECG in healthy people (of no clinical significance), increase in values of liver function laboratory tests (transaminases).

Uncommon side effects - effects that appear in -1-10 in 1,000 users
Changes in perception and feelings and appearance of psychotic symptoms, seizures, lack of coordination, disturbances in heart rhythm, increased blood pressure.

Very rare side effects - effects that appear in less than 1 in 10,000 users
Decrease in the number of white blood cells (leukopenia), decreased in the number of white blood cells called neutrophils (agranulocytosis), decrease in the number of blood platelets (thrombocytopenia), increased number of white blood cells called eosinophils (eosinophilia), serious and sudden allergic and hypersensitivity reactions (anaphylactic reactions), including a drop in blood pressure, syndrome of inappropriate ADH hormone (also called SIADH), abnormal EEG results (type of neurological test), neuroleptic malignant syndrome (a dangerous reaction characterized by high fever, muscle stiffness and decreased state of consciousness), glaucoma (loss of vision due to high pressure in the eye), cardiac conduction disorder, low blood pressure, allergic pneumonia (with and without an increase in eosinophils) that causes shortness of breath and cough, inflammation of the liver with or without jaundice, hair loss, haemorrhages beneath the skin, urinary retention, very high fever, oedema (swelling of the joints, hands or other parts of the body).

Side effects with unknown frequency (effects whose frequency has not yet been determined)
- suicidal behaviour and thoughts (suicidal behaviour and thoughts have been reported during treatment or shortly after treatment with clomipramine was stopped)
- inner restlessness and a constant urge to move
- repeated, involuntary and irregular movements
- muscle breakdown
- increase in the blood level of the hormone that produces milk (prolactin)
- serotonin syndrome, a syndrome caused due to an increase in serotonin, a naturally occurring substance in the brain, manifested by agitation, confusion, diarrhoea, fever, increased blood pressure, excessive sweating, rapid heartbeat, muscle twitching, seizures and unconsciousness
- delay or inability to ejaculate (in men)
- patients taking a medicine of this group (selective serotonin reuptake (SSRI), or tricyclic antidepressant)) are more likely to experience bone fractures.

After suddenly stopping the medicine or reducing the dose, withdrawal symptoms such as nausea, vomiting, abdominal pain, diarrhoea, insomnia, headache, nervousness and anxiety have been observed.

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 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or 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 your 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 below 25˚C, protect from moisture.

6. Additional information

In addition to the active ingredients, this medicine also contains:
Anafranil 25 mg:

sucrose, lactose monohydrate, talc, maize starch, silica colloidal anhydrous, stearic acid, magnesium stearate, glycerol 85%, hypromellose, vinylpyrrolidone, povidone, titanium dioxide (CI 77891, E171), polyethylene glycol 8000, cellulose microcrystalline, iron oxide yellow (CI 77492, E172).

Each tablet contains 15 mg lactose monohydrate and approximately 17 mg sucrose.

Anafranil SR 75 mg tablets:

calcium hydrogen phosphate dihydrate, polyacrylate dispersion 30%, calcium stearate, hypromelose, talc, silica, colloidal anhydrous, castor oil hydrogenated, pigment suspension white: titanium dioxide (CI 77891, E171), hypromelose (E464), pigment suspension red: iron oxide red (CI 77491, E172), hypromelose (E464).

What the medicine looks like and contents of the pack:
Anafranil 25 mg:
Light yellow, round, biconvex sugar-coated tablet.
Pack size: 30 tablets.

Anafranil SR 75 mg tablets:
Pink, capsule-shaped, biconvex, film-coated tablet, scored on both sides. One side debossed with C/G and the other G/D.
Pack size: 20 tablets.

Registration holder and importer's name and address: Tzamal Bio-Pharma, 20 Hamagshimim St., Petah Tikva.

Manufacturer's name and address: Pharmaand GmbH, Taborstrasse 1, 1020, Vienna, Austria.

Revised in December 2024.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Anafranil 25 mg: 108-06-24600-00
Anafranil SR 75 mg tablets: 053-91-26407-00

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