PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The 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

Sustained-release tablets, Divisible

Each tablet contains:

Clomipramine Hydrochloride 75 mg

Inactive ingredients: See chapter 6 'Further information' and chapter 2, section 'Important information about some of the ingredients of the medicine'.

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the 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.

1. WHAT IS THE MEDICINE INTENDED FOR?

Anafranil is used in adults to treat different types of depression and obsessive-compulsive disorders associated with compulsive behavior and thoughts. Mood, as well as physical symptoms, such as sleeplessness, dizziness, heart palpitations and other disturbances, improve.

Anafranil is also used to treat obsessive-compulsive disorders in children and adolescents over the age of 5.

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

Depression of varying origin

The use of Anafranil to treat states of depression of various causes and symptoms in children and adolescents (of ages 0-17 years) is not recommended as there is insufficient information on the safety and efficacy of Anafranil for treatment of this indication in children and adolescents.

Obsessive-compulsive disorder (OCD)

There is no experience in children younger than 5 years of age.

Therapeutic group

Tricyclic antidepressants, nonselective monoamine reuptake inhibitors.

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- If you have or have had hypersensitivity (an allergic reaction) to clomipramine, or any of the additional ingredients listed in chapter 6 'Further information' or to any other medicine from the tricyclic antidepressant group
- In combination with certain medicines to treat depression, such as monoamine oxidase (MAO) inhibitors or during the 14 days before or 14 days after treatment with MAO inhibitors
- In combination with antiarrhythmics, such as quinidine and propafenone
- If you have recently had a heart attack or if you suffer from a serious heart disease (congenital prolonged QT interval syndrome)

In the following conditions:

- Severe intoxication from central nervous system depressants (e.g., hypnotics, analgesics or psychotropics) or from alcohol
- Severe urinary retention
- Severe confusion (delirium)
- Untreated narrow-angle glaucoma (increased intraocular pressure)
- Prostatic hyperplasia with urinary retention
- Pyloric (the passage between the stomach and the duodenum) stenosis
- Paralytic ileus

Special warnings regarding use of the medicine

In certain circumstances, Anafranil should not be taken or should only be taken after a thorough medical evaluation. Therefore, inform the doctor if you suffer from or have suffered from any of the following disturbances or diseases:

- Tendency for epileptic seizures
- Heart rhythm disorders or other heart or blood vessel problems
- Other mental conditions
- Increased intraocular pressure (glaucoma)
- Liver or kidney disease
- Changes in blood cell count
- Intoxication (e.g., from medicines)
- Gastric emptying disorders
- Difficulties passing urine or an enlarged prostate
- Overactive thyroid gland or taking thyroid medication at the same time with Anafranil
- Alcohol addiction
- Frequent constipation or bowel blockage
- Fainting
- Change in mood from depression to extreme euphoria
- If you have suicidal thoughts
- If you suffer from schizophrenia
- If you are about to undergo electroconvulsive therapy (ECT)
- If you take certain medicines to treat depression, e.g., selective serotonin reuptake inhibitors (SSRIs) (such as fluoxetine) or serotonin and noradrenaline reuptake inhibitors (SNaRIs), other tricyclic antidepressants and lithium
- If you are suffering from hypokalemia (low concentrations of potassium in the blood)

Further safety measures

- It is important that you and your family or caregivers discuss with the doctor any change in mood during the course of treatment with Anafranil.
- If you wear contact lenses and suffer from eye irritation, inform your doctor.
- Before every surgical procedure or before starting dental treatment, inform the doctor or the dentist that you are taking Anafranil.
- Anafranil may cause your skin to be more sensitive to sunlight. Therefore, avoid direct exposure to sunlight, wear sunglasses, and protect the skin with appropriate clothing.
- Tell your doctor or pharmacist if you experience fainting, any other disease, any allergies, sugar intolerance (e.g., lactose, sucrose) or are taking any other medicine (including non-prescription) or applying any medicines externally.

Tests and follow-up

It is important that your doctor regularly monitor the progress of your treatment so that he can adjust the dose and consequently reduce the side effects.

Your doctor may also perform blood tests, measure your blood pressure and check your heart and liver functions.

Anafranil may cause dry mouth, which may increase the risk of caries. Therefore, during prolonged treatment, dental examinations should be performed regularly.

Children and adolescents

The 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).

Information for families and caregivers

When Anafranil is given to children and adolescents, behavioral changes should be looked out for.

The symptoms of depression, particularly suicidal behavior, may get worse during the course of treatment with Anafranil. If they worsen, contact the doctor immediately.

There have been reports of an increase in the frequency of behavioral 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 was observed in data from clinical trials.

Treatment must not be stopped suddenly, rather, only in consultation with the doctor, since withdrawal symptoms may occur.

Elderly patients

Elderly patients generally need lower dosages 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.

Pregnancy and breastfeeding

Inform the doctor if you are pregnant, planning to become pregnant or are breastfeeding.

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.

The active ingredient of Anafranil passes into breast milk and mothers taking Anafranil are therefore advised not to breastfeed.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular if you are taking:

- Medicines for the heart or blood pressure
- Medicines that affect the central nervous system (such as: barbiturates, benzodiazepines, surgical anesthetics)
- Other antidepressants (such as: SSRIs or SNaRIs)
- Sedatives
- Epilepsy medicines (such as: barbiturates or valproic acid, carbamazepine and phenytoin)
- Hypnotics (such as: benzodiazepines)
- Strong analgesics (opiates)
- Medicines for preventing blood clotting (anticoagulants)
- Medicines for asthma or allergies
- Medicines for Parkinson's disease
- Thyroid medicines
- Medicines with the active ingredient cimetidine, for excessive secretion of gastric acid or gastric ulcers
- Hormonal contraceptives (birth control pills)
- Estrogens
- Methylphenidate (primarily used for attention deficit hyperactivity disorder [ADHD])
- Certain medicines to reduce blood lipids (ion-exchange resin)

Since many medicines may interact with Anafranil, it may be necessary to adjust the dose or stop treatment with one of the medicines.

Use of Anafranil and food

- Grapefruit, grapefruit juice, cranberry juice – may affect how the medicine works

Driving and operating machinery

This medicine may impair your responses, your ability to drive and your ability to use tools or machines.

Anafranil may cause you to be sleepy, reduce your alertness or cause blurred vision. If this happens to you, avoid driving a vehicle, operating machinery or engaging in any activity that requires full alertness. These effects may be increased by other medicines or alcohol.

Children should be cautioned against riding a bicycle or playing near the road, and the like.

Alcohol consumption

It is recommended to avoid drinking alcohol during the course of treatment, as Anafranil may reduce alcohol tolerance.

Smoking

Inform your doctor of changes in smoking habits.

Important information about some of the ingredients of the medicine

Anafranil 25 mg, coated tablets: The tablet contains lactose and sucrose. If you have been told by the doctor that you have an intolerance to certain sugars (e.g., lactose, sucrose), refer to the doctor before taking Anafranil 25 mg, coated tablets.

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

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Dosage
The dosage and treatment regimen will be determined by the doctor only.

Do not exceed the recommended dose.

Method of administration
Anafranil SR 75 mg tablets:
The tablets can be halved but should not be chewed.
Anafranil 25 mg: There is no information about halving or chewing the tablet.
Anafranil can be taken with or without food.

If you accidentally took a higher dosage
The following symptoms of overdose usually appear within a few hours: heavy drowsiness; poor concentration; dulled senses; fast, slow, or irregular heartbeat; restlessness and agitation; loss of muscle coordination and muscle stiffness; shortness of breath; seizures; vomiting, fever.
If you took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you. Medical treatment may be necessary.
An overdose of this medicine is particularly dangerous in young children.

If you forget to take the medicine
Use this medicine at set intervals, as determined by the attending doctor.
If you forget to take this 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 dose, skip the missed dose and continue with the regular treatment program.
Adhere to the treatment as recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you stop taking the medicine
Treatment of depression and obsessive-compulsive disorder require long-term treatment with Anafranil. The duration of treatment is determined by the doctor only. The doctor may want to gradually lower the dosage before completely stopping treatment in order to avoid worsening of the condition and to reduce the risk of medicine withdrawal symptoms, such as: filling sick, abdominal pain, diarrhea, difficulty falling asleep, anxiety or nervousness, headaches, nausea and generalized discomfort.

Do not take medicines in the dark! Check the label and the dose each time you take medicine.

Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Anafranil may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Side effects that require special attention
- Disturbances in body fluid quantities and salt levels, accompanied with symptoms such as confusion, hallucinations, seizures and brain edema (swelling due to accumulation of fluids in the brain) may occur. In such cases, refer to a doctor immediately.
- Very rarely, neuroleptic malignant syndrome may occur. The main symptoms are fever, irregular heartbeat, consciousness disturbances and muscle stiffness. In such cases, refer to a doctor immediately.
- Medicines such as Anafranil, alone or in combination with other medicines, may cause serotonin syndrome. Typical symptoms of this syndrome are: fever, muscle spasms, seizures, restlessness, confusion and lack of consciousness. In such cases, refer to a doctor immediately.

Additional side effects

Very common side effects – effects that occur in more than 1 user in 10
- Light-headedness
- Temporary tiredness
- Dizziness
- Tremor
- Restlessness
- Increased appetite
- Weight gain
- Dry mouth
- Disturbances passing urine
- Muscle spasms
- Inability to focus vision
- Blurred vision
- Headache
- Sweating
- Constipation

Common side effects – effects that occur in 1-10 in 100 users
- Confusion with spatial disorientation and hallucinations
- Concentration disorders
- Speech disorders
- Sleep disturbances
- Anxiety
- Increased energy and elated mood
- Over-excitedness
- Aggressiveness
- Behavioral disorders
- Poor memory
- Yawning
- Insomnia
- Nightmares
- Numbness or a tingling sensation in the arms and legs
- Muscle weakness
- Muscle stiffness
- Hot flushes
- Dilated pupils
- Heart palpitations
- Low blood pressure combined with dizziness upon changing position
- Worsening depression
- Nausea
- Sensitivity to light
- Allergic skin reactions
- Itchy skin
- Increased laboratory test values
- Sexual function and drive (libido) disturbances
- Ringing in the ears

Uncommon side effects – effects that occur in 1-10 in 1,000 users
- Increased blood pressure
- Seizures
- Heart rhythm disorders
- Loss of appetite
- Movement and coordination disturbances
- Changes in perception and feelings
- Vomiting
- Gastrointestinal diseases
- Diarrhea
- Enlargement of the breast glands and increased milk secretion
- Unpleasant taste in the mouth

Very rare side effects – effects that occur in less than one user in 10,000
- High fever
- Decrease in the number of white blood cells (leukocytopenia), decrease in the number of blood platelets (thrombocytopenia), decrease in the number of neutrophil white blood cells (agranulocytosis) or increased number of eosinophil white blood cells (eosinophilia)
- Bleeding under the skin
- Hypersensitivity reaction (allergy), including shock, with reactions of the lungs and the entire body
- Movement disorders
- Glaucoma
- Conduction disorders of the heart
- Hepatitis with or without jaundice
- Edema (swelling of the joints, hands or other parts of the body)
- Hair loss
- Insufficient urine output
- EEG changes
- Pneumonia

Side effects of unknown frequency (effects whose frequency has not yet been determined)
- 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)
- Delayed or no ejaculation (in men)

The majority of the side effects listed above go away during treatment, after the adjustment period to the preparation.
If these effects continue or become bothersome, refer to a doctor.
- There have been reports of an increase in the frequency of behavioral disorders – including a greater risk of suicidal thoughts, self-harm and suicide – in children and adolescents with depression or other psychiatric diagnoses who are being treated with antidepressants
- An increased risk of bone fractures in patients aged 50 and older taking this type of medicine was observed

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning.
Do not induce vomiting unless explicitly instructed to do so by the doctor.
Do not use the medicine after the expiry date (exp. date) that appears on the package.
The expiry date refers to the last day of that month.

Storage conditions
Store below 25°C, protect from moisture.

6. FURTHER INFORMATION

In addition to the active ingredient, the 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 the contents of the package

Anafranil 25 mg:
Sugar-coated, light yellow, round and biconvex tablet.
Package size: 30 tablets.

Anafranil SR 75 mg tablets:
Pink, film-coated, capsule-shaped, convex tablet with a score line on both sides. CG is imprinted on one side and GD on the other side.
Package size: 20 tablets.

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.
Revised in October 2021 according to MOH guidelines.
Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Anafranil 25 mg:
108 06 24600
Anafranil SR 75 mg tablets:
053 91 26407

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