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

Entumin
Tablets

Active ingredient
Each tablet contains:
clotiapine 40 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 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?
For the treatment of severe mental and emotional disorders (neuroleptic).

Therapeutic group:
Antipsychotic.

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

- If you are sensitive (allergic) to the active ingredient (clotiapine) or to any of the other ingredients in this medicine (see section 6).
- If you have a history of epilepsy and/or factors predisposing to epilepsy (brain injuries from various causes, concomitant use of other medicines for psychosis, withdrawal from alcohol or benzodiazepines [medicines which reduce anxiety and tension]).
- If you are in a comatose state.
- If you have major CNS depression (the central nervous system [CNS] is made up of the brain and the spinal cord. When the function of the CNS becomes slower, we call it CNS depression) or post-encephalitic states (pathological condition resulting from inflammation of the brain).
- If you have increased pressure inside the eye (narrow angle glaucoma).
- If you are breastfeeding.
- In children below the age of 16 years.

Special warnings about using this medicine
Before treatment with Entumin, tell your doctor:
- If you suffer from heart disease (including an abnormality called prolonged QT).
- If you have any of the following problems: prostate disease, disorder of the bowel (chronic constipation), kidneys or liver, Parkinson's disease, low blood pressure (hypotension).
- In elderly patients, particularly if they have dementia.
- If you suffer from movement disorders (tardive dyskinesia).
- If you suffer from diabetes or have risk factors for diabetes.

- If you have, or someone else in your family has, a history of blood clots, as medicines in this class have been linked to the formation of blood clots.
- If you have risk factors for cerebrovascular accident (also known as “stroke”, occurring when the blood circulation is suddenly interrupted in a part of the brain).
- If you have a history of hyperprolactinaemia (too much prolactin, a hormone triggering milk secretion, in the blood) or a prolactin-dependent tumour, for example breast cancer. In this case, your doctor needs to monitor you closely during treatment.
- If you suffer from liver or kidney disease, only take this medicine on your doctor’s advice. Your doctor may arrange additional examinations while you are taking this medicine.

Entumin can lower the seizure threshold.

Treatment should be stopped gradually.

During treatment:
You must inform your doctor immediately in the following cases:

- If you experience rigidity of your muscles combined with impaired consciousness and fever (neuroleptic malignant syndrome). In this case, you must stop the treatment immediately and inform your doctor.
- If you have fever or notice any other sign of infection. In exceptional cases, this medicine can cause a fall in your white blood cell count, which increases the likelihood of infection.
- If you have persistent constipation, together with bloating and abdominal pain. In very rare cases, this medicine can cause your bowel transit to stop. Your doctor will prescribe you medicine to prevent further complications.
- If you experience excessive drowsiness.

Children and adolescents
Entumin must not be administered to children aged under 16 years.

Tests and follow-up:
- During the period of treatment with this medicine, blood pressure monitoring should be conducted in elderly patients.
- In patients with a history of low white blood cell levels or drug induced leukopenia/neutropenia, the doctor will conduct frequent complete blood count monitoring in the first treatment months.
- In patients with neutropenia, the doctor will closely monitor you for fever or other infection symptoms.

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:

Many medicines influence (or are influenced by) Entumin treatment.
You must inform your doctor if you are taking any other medicine (such as medicines to treat raised blood pressure, heart rhythm problems, depression, allergies, Parkinson’s disease, sleep problems or malaria, tranquillisers, lithium, neuroleptics) and consult your doctor or pharmacist before taking any other medicine.

Using this medicine and food
This medicine can be taken with and without food.

Using this medicine and alcohol consumption
Avoid drinking alcohol during the period of treatment with this medicine.

Pregnancy, breastfeeding, and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, consult your doctor or pharmacist before taking this medicine.

Pregnancy
Tell your doctor as soon as the pregnancy is confirmed. Your doctor is the most appropriate person to decide about prescribing Entumin during pregnancy.
The following symptoms may occur in neonates born to mothers who have taken Entumin during the last trimester (last 3 months of their pregnancy): tremor, muscle stiffness and/or muscle weakness, somnolence, agitation, breathing problems and feeding difficulties. If your baby demonstrates any of the above symptoms, contact a doctor.

Breastfeeding
Do not use Entumin during breastfeeding. The metabolites of Entumin are excreted in breast milk.

Fertility
There are no clinical data on fertility. In a toxicity study in dogs, effects on the testes (seminiferous tubule changes with a reduction in the sperm count) were observed, but the clinical relevance of these results is not known.

Driving and using machines
Avoid driving or operating machines, especially at the start of treatment, as Entumin may cause drowsiness and reduce your reaction capacity.

Important information about some of this medicine's ingredients
The tablets contain lactose. If you have been told in the past by a doctor that you have an intolerance to certain sugars, consult your doctor before starting treatment with this medicine.

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 maximal daily dosage of 360 mg in divided doses.
- In underweight patients, patients with liver or kidney disease and in the elderly, treatment should be started at lower dosages, and the dosage should be gradually increased.

Do not exceed the recommended dose.
- Do not chew!
- Swallow the medicine with some water.
- The tablet can be split at the score line and crushed.

If you have accidentally taken a higher dose, you may experience somnolence or significant agitation, coma, seizures, difficulties breathing, blood pressure drop, very rapid or irregular heart rate, tremor, muscle stiffness.
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.

If you forgot to take Entumin
Do not take a double dose to compensate for the forgotten dose.

If you stop using Entumin
The treatment must be stopped gradually. Even if your health improves, do not stop taking this medicine without consulting your doctor.

Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> 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 Entumin may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Consult your doctor <u>immediately</u> if you notice any of the following symptoms:
- Blood clots in the veins, particularly in the legs (symptoms include swelling, pain and redness in the legs), which may circulate through the blood vessels to the lungs, causing chest pain and breathing difficulties (frequency not known).
- A combination of fever, impaired consciousness and muscle stiffness (neuroleptic malignant syndrome) (frequency not known).
- You have dementia and experience a sudden change in your mental state or a sudden onset of weakness or numbness in your face, arms or legs, particularly on one side, or difficulties speaking, even for a short period of time. These may be signs of a cerebrovascular accident (frequency not known).
- You have tardive dyskinesia (jerky or shaky movements of your face, tongue or other parts of your body which you cannot control) (uncommon). Tell your doctor immediately if you experience involuntary rhythmic movements of your tongue, mouth and face. It may be necessary to stop the treatment.

Elderly people with dementia treated with conventional antipsychotics have a slightly increased risk of death compared with those who are not treated.

Additional side effects
Uncommon side effects (affect less than 1 in 100 users):
- blurred vision
- agitation and confusion
- feeling of dry mouth, constipation or even absence of bowel transit
- low blood pressure when standing up from lying (or sitting) down (orthostatic hypotension)

- difficulty keeping still fear of sitting down
- movement disorders (dyskinesia)
- involuntary muscle movements (dystonia)
- prolonged QTc (the QT interval is a measurement recorded in an electrocardiogram, which is used to evaluate certain electrical properties of the heart) (see section 2, 'Special warnings about using this medicine').

Rare side effects (affect less than 1 in 1000 users):
- rapid and irregular heartbeat, even at rest, palpitations.

Side effects of unknown frequency (the frequency of these effects has not been established yet)
- changes in the levels of certain blood cell lines, including a major reduction in the number of certain white blood cells, which can lead to serious infections (agranulocytosis) or a reduction in the platelet count, which can lead to bruising or bleeding
- weight gain
- a change in the blood sugar level, development or worsening of diabetes
- a change in the levels of fats (triglycerides) and cholesterol in the blood
- sedation and drowsiness
- fainting
- fatigue
- inflammation of the pancreas
- gastroenteritis
- urine retention
- sweating
- hyperprolactinaemia (too much prolactin, a hormone triggering lactation, in the blood) with associated menstrual problems, fertility problems, reduced libido, erectile dysfunction, development of mammary glands in men
- neonatal abstinence syndrome (see section 2, 'Pregnancy')
- tremor, muscle rigidity (parkinsonism)
- seizures (involuntary contractions of one or several muscles)
- abnormal increase in the speed and range of movements
- vision problems (myopia, etc.)
- oedema
- fever
- allergic reactions which can cause skin redness, itching (hypersensitivity), as well as a heightened skin reaction when you are exposed to sunlight or ultraviolet rays
- sudden cardiac death
- EEG changes (electroencephalogram [EEG]: neurological examination enabling recording of the electrical activity of the brain by placement of electrodes on the scalp)
- paralytic ileus
- rash.

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.

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

- Do not store above 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

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

Lactose, maize starch, cellulose microcrystalline, gelatin, colloidal anhydrous silica, paraffin liquid, talc, magnesium stearate.

What the medicine looks like and contents of the pack:

Round and flat white to yellowish tablets, with a slanted edge and a score line on one side, packed in a blister (tray) package.
Each pack contains 30 or 500 tablets.
Not all pack sizes may be marketed.

Registration holder's name and address:

Taro International Ltd., 14 Hakitor St., Haifa Bay 2624761

Manufacturer's name and address:

DELPHARM L'Aigle,
Zone Industrielle 1, Route De Crulai, L'Aigle, 61300, France

Revised in November 2024.

Registration number of the medicine in the Ministry of Health National Drug Registry:

023.40.21411.00

For further information about the medicinal product and for updated patient leaflets in Hebrew, Arabic and English, please scan the code:

https://israeldrugs.health.gov.il/#!/medDetails/023%2040%2021411%2000

For a printed copy of the patient information leaflet in English, please contact the registration holder by email Info@taro.com or by phone 1-800-464-664.