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

This medicine is dispensed by a doctor's prescription only

Cipramil® 20 mg Tablets
Cipramil® 40 mg Tablets

Composition:
Each film-coated tablet of Cipramil 20 mg contains:
The active ingredient Citalopram Hydrobromide, equivalent to 20 mg Citalopram

Each film-coated tablet of Cipramil 40 mg contains:
The active ingredient Citalopram Hydrobromide, equivalent to 40 mg Citalopram

Inactive ingredients: see section 6 and section "Important information about some of the ingredients of Cipramil".

- **Read the entire leaflet carefully before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or the pharmacist.
- **It is recommended to let a family member or another person who is close to you to read this leaflet.**
- This medicine was prescribed for you. Do not pass it on to others. It can harm them even if it seems to you that their medical state is similar.

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
Antidepressants and anti-anxiety medications increase the risk of suicidal thoughts and behaviour in children, adolescents, and young adults up to 25 years old.
In patients of all ages who start taking this medicine, the patients and their relatives should monitor behavioural changes such as worsening of depression, suicidal thoughts, aggression and other similar changes. In case such changes occur, contact your doctor immediately.

1. WHAT IS THE MEDICINE INTENDED FOR?

Therapeutic activity: for the treatment of depression and panic disorder.
Cipramil belongs to a group of antidepressants called Selective Serotonin Reuptake Inhibitors (SSRIs). These medicines increase the serotonin level in the brain.

Disturbances in the serotonin-system in the brain are considered an important factor in the development of depression and related diseases.

Pharmacotherapeutic group: Selective Serotonin Reuptake Inhibitors (SSRI).

2. BEFORE USING THE MEDICINE

Do not use Cipramil if:

- You are hypersentive (allergic) to citalopram or to any of the other ingredients of the medicine (see "inactive ingredients" in section 6). Consult your doctor if you think you might be.
- You concomitantly take medicines which belong to a group called monoamine oxidase inhibitors (MAOIs) such as: phenelzine, iproniazid, isocarboxazid, nialamide, tranylcypromine and moclobemide (used in the treatment of depression) selegiline (for treatment of Parkinson´s disease), and linezolid (an antibiotic). Even if you have finished taking one of the following MAOIs: phenelzine, iproniazid, isocarboxazid, nialamide or tranylcypromine you will need to wait 2 weeks before you start taking your Cipramil tablets.

  One day must elapse after you have finished taking moclobemide. After stopping Cipramil you must allow 1 week before taking any MAOI.

- if you are born with or have had an episode of abnormal heart rhythm (seen at ECG; an examination to evaluate how the heart is functioning).
- if you take medicines for heart rhythm problems or that may affect the heart's rhythm (see **Drug interactions** below).

Special warnings regarding use of the medicine

Before using Cipramil, tell the doctor if you have any medical problems, especially if you have:
- History of bleeding disorders or have ever suffered from bleeding in the stomach or intestine, or if you are pregnant (see 'Pregnancy, breast-feeding and fertility').
- Liver disease.
- Kidney disease.
- Diabetes (there may be a need to adjust the dosage of the medicines for diabetes).
- Epilepsy or a history of seizures or fits.
- Mania or panic disorder
- Low blood levels of sodium
- Electroconvulsive treatment (ECT).
- You suffer or have suffered in the past from heart problems or if you have recently had a heart attack.
- You have a low resting heart-rate and/or you know that you may have salt depletion as a result of prolonged severe diarrhoea and vomiting (being sick) or usage of diuretics (water tablets).
- Experienced a fast or irregular heartbeat, fainting, collapse or dizziness on standing up which may indicate abnormal functioning of the heart rate.
- If you have or have previously had eye problems, such as certain kinds of glaucoma (increased pressure in the eye).

Please consult your doctor, even if these statements were applicable to you at any

time in the past.

Please note

- Some patients with manic-depressive illness may enter into a manic phase. This is characterized by unusual and rapidly changing ideas, inappropriate happiness and excessive physical activity. If you experience this, contact your doctor.
- Symptoms such as restlessness or difficulty to sit or stand still can also occur during the first weeks of the treatment. Tell your doctor immediately if you experience these symptoms.
- Medicines like Cipramil (so called SSRIs/SNRIs) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping treatment.

Special information relating to your disease
As with other medicines used to treat depression or related diseases, the improvement is not achieved immediately. After the start of Cipramil treatment it may take several weeks before you experience any improvement. In the beginning of the treatment certain patients may experience increased anxiety, which will disappear during continued treatment. Therefore, it is very important that you follow exactly your doctor's orders and do not stop the treatment or change the dose without consulting your doctor.

Thoughts of suicide and worsening of your depression or anxiety disorder:

If you are depressed and/or have anxiety disorders 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.**

It is recommended to tell a relative or close friend that you are depressed or have an anxiety disorder, 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.

Children and adolescents under 18 years of age
Cipramil should normally not be used for children and adolescents under 18 years. Also, you should know that patients under 18 have an increased risk of side-effects such as suicide attempts, suicidal thoughts and hostility (predominately aggression, oppositional behaviour and anger) when they take this class of medicines. Despite this, your doctor may prescribe Cipramil for patients under 18 because he/she decides that this is in their best interest. If your doctor has prescribed Cipramil for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any symptoms listed above develop or worsen when patients under 18 are taking Cipramil. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Cipramil in this age group have not yet been demonstrated.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
Medicines may affect the action of other medicines and this can sometimes cause serious adverse reactions. Please tell your doctor or pharmacist if you are taking, have taken or might take any other medicines. This includes other medicines for depression (see section:" **Do not use Cipramil if**").

- The herbal remedy St John's wort (Hypericum perforatum). This should not be taken at the same time as Cipramil.
- Monoamine oxidase inhibitors (MAOIs). These should not be taken at the same time as Cipramil (see section:" **Do not use Cipramil if**").

Tell your doctor if you are taking any of the following medicines:

- Linezolid (an antibiotic).
- Sumatriptan (used to treat migraine) or tramadol and buprenorphine and similar medicines (strong pain killers). Taking these medicines together with Cipramil can lead to serotonin syndrome, a potentially life-threatening condition. The syndrome may be associated with 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.
- lithium (used to prevent and treat mania) and tryptophan (an antidepressant) .
- Pimozide (a neuroleptic). This should not be taken at the same time as Cipramil.
- imipramine and desipramine (used to treat depression).
- Medicines containing selegiline (used to treat Parkinson's disease).
- cimetidine lansoprazole and omeprazole (used to treat stomach ulcers) , fluconazole (used to treat fungal infections), fluvoxamine (antidepressant) and ticlopidine (used to reduce the risk of stroke). These may cause increased blood levels of citalopram.

- Mefloquine (used to treat malaria).
- Bupropion (used to treat depression).
- Medicines known to affect the blood platelets (e.g. anticoagulant drugs used to treat or prevent blood clots; aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and diclofenac used as painkillers and some antipsychotic drugs and tricyclic antidepressants).
- Metoprolol, a beta blocker used to treat migraine, some heart conditions and high blood pressure. The effects of either drug could be increased, decreased or altered.
- neuroleptics (used in the treatment of schizophrenia).

Do not take Cipramil if you take medicines for heart rhythm problems or medicines that may affect the heart's rhythm, e.g. such as Class IA and III antiarrhythmics, antipsychotics (e.g. phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobial agents (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, anti-malarial treatment particularly halofantrine),

certain antihistamines (astemizole, mizolastine). If you have any further questions about this you should speak to your doctor.

Use of the medicine and food
The medicine can be taken with or without food.

Use of the medicine and alcohol consumption
As with all antidepressants, it is sensible to avoid drinking alcohol whilst receiving treatment although Cipramil has not been shown to increase the effects of alcohol.

Pregnancy, breast-feeding and fertility

Pregnancy
If you take Cipramil near the end of your pregnancy there may be an increased risk of heavy vaginal bleeding shortly after birth, especially if you have a history of bleeding disorders. Your doctor or midwife should be aware that you are taking Cipramil so they can advise you. Ask your doctor or pharmacist for advice before taking any medicine. If you are pregnant, think you might be pregnant, or are trying to become pregnant, tell your doctor.
Do not take Cipramil if you are pregnant, unless you consulted with your doctor and discussed the risks and benefits involved.
Make sure your midwife and/or doctor know you are on Cipramil.
When taken during pregnancy, particularly in the last 3 months of pregnancy, medicines like Cipramil may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (PPHN), making the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born. If this happens to your baby you should contact your midwife and/or doctor immediately. Also, if you take Cipramil during the last 3 months of your pregnancy and until the date of birth you should be aware that the following effects may be seen in your newborn: fits, being too hot or cold, feeding difficulties, vomiting, low blood sugar, stiff or floppy muscles, overactive reflexes, tremor, jitteriness, irritability, lethargy, constant crying, sleepiness or sleeping difficulties. If your newborn baby gets any of these symptoms please contact your doctor immediately.

Breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine. If you are breast- feeding, ask your doctor for advice. Do not breast feed while taking this medicine, because small amounts might pass into the breast milk.

Fertility

Citalopram, the active ingredient in Cipramil, has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.

Driving and using machines
Cipramil does not usually affect the ability to carry out normal daily activities. However, if you feel dizzy or sleepy when you start to take this medicine, you should

be careful when driving, operating machinery or performing jobs that need you to be alert until these effects wear off.

Important information about some of the ingredients of Cipramil
Information about sodium content

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Cipramil contains lactose.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions.
You should check with the doctor or pharmacist if you are not sure.
The dosage and treatment regimen will be determined by the doctor only. The usual dose is:
Depression: 20 mg per day. The dose may be increased by the doctor to a maximum of 40 mg per day.
Panic disorder: The starting dose is 10 mg per day for the first week before increasing the dose to 20 mg per day. The dose may be increased by the doctor to a maximum of 40 mg per day.

Elderly patients (above 65 years of age): the dose should be decreased to half of the recommended dose: 10 mg to 20 mg per day. Maximal dose: 20 mg per day.
Patients with impaired liver function: the dose should be decreased: a maximal dose of 20 mg per day.
Children and adolescents under 18 years of age: Cipramil should not be given to children and adolescents. For additional information see "2. Before using the medicine".

Do not exceed the recommended dose.

Directions for use:
Take Cipramil once a day as a single daily dose.
Cipramil can be taken any time of the day with or without food.
Do not chew the medicine (because it has a bitter taste). Swallow this medicine with a little water.
Do not retain this medicine in the mouth for a period longer than that required for swallowing.
It is possible to divide the tablet.

If you mistakenly took a higher dosage:
Overdose symptoms (some of which could be life-threatening):
Irregular heartbeat, convulsions, changes in the heart rate, sleepiness, unconsciousness, vomiting, tremor, decreased blood pressure, increased blood pressure, nausea, serotonin syndrome (see section "4.side effects"), agitation, dizziness, dilated pupils of the eye, blue-ish skin, hyperventilation.

If you accidentally took an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to the doctor or to a hospital emergency room, and

bring the package of the medicine with you, even if you did not observe any of the symptoms described above.
Do not induce vomiting, unless specifically advised to by a doctor!

This medicine is to be taken at specific time intervals as determined by the attending doctor.
If you forget to take this medicine at the specified time, take the dose as soon as you remember, but never take a double dose to compensate for a missed one.

Complete the full course of treatment as instructed by the doctor.

Duration of treatment:
Similarly to other drugs for the treatment of depression and similar diseases, the improvement is not achieved immediately. After commencing the treatment, a few weeks (2-4 weeks) may pass before you feel an improvement in your condition. During the beginning of the treatment some patients may feel an increase in the feeling of anxiety that will subside in the duration of treatment. Therefore, it is important to take the drug according to the doctor's instructions and not stopping or changing the dosage without consulting the doctor.

If you stop taking the medicine: Abrupt cessation of the medicine may cause symptoms such as: dizziness, feelings like pins and needles, sleep disturbances (vivid dreams, nightmares, inability to sleep), feeling anxious, headaches, feeling sick (nausea), vomiting, sweating, feeling restless or agitated, tremor, feeling confused or disorientated, feeling emotional or irritable, diarrhoea, visual disturbances, fluttering or pounding heartbeat (palpitations).

The duration of treatment with this drug is different between patients and it is usually at least 6 months. Patients with reoccurring depressions may be treated with this drug for a long period of time and even for several years.
Even if your health improves, do not stop treatment with the medicine without consulting a doctor or pharmacist: Your illness may resume and also in case it is

decided to stop the treatment it should be done gradually in order to prevent side effects.

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

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

4. Side effects:

As with all medicines, use of Cipramil may cause side effects in some users. Do not be alarmed when reading the list of side effects; you may not experience any of them.
Several of the effects listed below can also be symptoms of your illness and may disappear as you start to get better.

Serious side effects

Stop taking Cipramil and refer to the doctor immediately if the following symptoms appear:

- Difficulty in breathing.
- Swelling of the face, lips, tongue or throat that causes difficulty in swallowing or breathing.
- Severe itching of the skin (with raised lumps).
- Fast, irregular heart beat, fainting which could be symptoms of a life-threatening condition known as torsades de pointes.

If you notice any of the following symptoms you should contact your doctor immediately as your dose may need to be reduced or stopped:

- You start having fits for the first time or fits that you have suffered from in the past become more frequent.
- Your behaviour changes because you feel elated or over excited.
- You experience high fever, agitation, confusion, trembling or abrupt contractions of muscles. These may be signs of a rare condition called serotonin syndrome.
- Tiredness, confusion and twitching of your muscles. These may be signs of a low blood level of sodium (hyponatraemia).

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

The following side effects are often mild and usually disappear after a few days' treatment.

<u>Very common side effects (may affect more than 1:10 people):</u>

- Sleepiness
- Difficulty in sleeping
- Headache
- Changes in your sleeping pattern
- Loss of body strength, weakness
- Increased sweating

- Dry mouth (which increases the risk of caries, therefore you should brush your teeth more often than usual).
- nausea (feeling sick).

Common side effects (may affect up to 1 in 10 people):
decreased appetite, agitation, decreased sexual drive, anxiety, nervousness, confusion, abnormal dreams, reduced emotions, indifference (apathy), tremor, tingling or numbness in the hands or feet, dizziness, problems concentrating, migraine, loss of memory (amnesia), ringing in the ears (tinnitus), palpitations, yawning, blocked or runny nose (rhinitis), diarrhea, vomiting, constipation, stomach pain, flatulence (wind), drooling, itching, pain in muscle and joints, problems with ejaculation and erection in men, failure to achieve an orgasm in women, tiredness, prickling of the skin, decreased weight.

Uncommon side effects (may affect up to 1 in 100 people):
cutaneous bleeding disorder (easily bruising), increased appetite, aggression, hallucinations, mania, fainting, enlarged pupils, fast heart beat, slow heart beat, nettle rash, loss of hair, rash, sensitivity to sunlight, difficulties urinating, excessive menstrual bleeding, swelling of the arms or legs, increased weight.

Rare side effects (may affect up to 1 in 1000 people):
Increased sex drive, convulsions, involuntary movements, taste disturbance, bleeding, coughing, hepatitis, feeling unwell (malaise).

Some patient have reported (side effects frequency not known):
Heavy vaginal bleeding shortly after birth (postpartum haemorrhage), see ‘Pregnancy, breast-feeding and fertility’ in section 2 for more information.; thoughts of harming yourself or thoughts of killing yourself (see also section: "2. Before using the medicine"); reduction in blood platelets (thrombocytopenia)

which increases risk of bleeding or bruising, rash (hypersensitivity), hypokalaemia: low blood levels of potassium which can cause muscle weakness, twitching or abnormal heart rhythm; panic attack, grinding one’s teeth, restlessness, unusual muscle movements or stiffness, akathisia (involuntary movements), low blood pressure, nosebleed, bleeding disorders including skin and mucous bleeding (ecchymosis), sudden swelling of skin or mucosa, in men - painful erections, flow of milk in men and women that are not nursing, irregular menstrual periods, abnormal liver function tests, an increased risk of bone fractures has been observed in patients taking this type of medicines, abnormal heart rhythm.

SSRIs can, very rarely, increase the risk of bleeding, including stomach or intestinal bleeding. Let your doctor know if you vomit blood or develop black or blood stained stools.

Also let your doctor know if you continue to have other symptoms associated with your depression. This might include hallucinations, anxiety, mania or confusion.

Any side effects that do occur will usually disappear after a few days. If they are troublesome or persistent, if any of the side effects gets worse, or if you suffer from any side effects not listed in the leaflet, consult the doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Adverse Drug Reactions Report” that appears on the home page of the Ministry of Health web site (www.health.gov.il), which leads to an online form for reporting side effects. Alternatively you can use following link:

https://sideeffects.health.gov.il/

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and all other medicines, must be stored in a closed place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting without explicit instructions from 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 at a temperature below 30°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

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

Inactive ingredients:

Maize starch, Lactose Monohydrate, Microcrystalline Cellulose, Copovidone, Glycerol 85%, Croscarmellose Sodium, Hypromellose, Magnesium Stearate, Titanium Dioxide (E171), Macrogol 400.

Each Cipramil 20 mg tablet contains 23.1 mg Lactose Monohydrate.

Each Cipramil 40 mg tablet contains 46.1 mg Lactose Monohydrate.

- **What the medicine looks like and contents of the pack:**

Cipramil 20 mg: an oval film-coated tablet, white, scored, marked with “C” and “N”

Cipramil 40 mg: an oval film-coated tablet, white, scored, marked with “C” and “R”

The tablets are presented in packs that contain 14, 28, 56, 98 and 100 tablets. Not all pack sizes may be marketed.

License holder: Lundbeck Israel Ltd., 11 Galgaley Haplada, P.O.B. 13105, Herzliya 4672211

Email address: Israel@lundbeck.com

Manufacturer: H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark.

Revised in January 2023 according to MoH guidelines.

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

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Cipramil 40 mg 142 50 32025