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

Ebixa 5 mg/pump actuation
oral solution

Composition:
Active ingredient and its quantity: Memantine Hydrochloride 10 mg/g.
Each pump actuation (one downward stroke) delivers 0.5 ml of solution which contains 5 mg of memantine hydrochloride.
Inactive ingredients: See list in section 6 and section "important information about some of the ingredients of the medicine".

- **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.
- This medicine was prescribed for the treatment of your ailment. Do not pass it on to others. It can harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Ebixa is intended for the treatment of moderate to severe Alzheimer's disease.

Therapeutic group: NMDA receptor antagonist.

Ebixa belongs to a group of medicines for the treatment of dementia. Memory loss in Alzheimer's disease is due to a disturbance of message signals in the brain. The brain contains so-called N-methyl-D-aspartate (NMDA)-receptors that are involved in transmitting nerve signals important in learning and memory. Ebixa acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient or to any of the other ingredients which the medicine contains (see list of inactive ingredients in section 6).

Special warnings regarding use of the medicine

Before using Ebixa, tell the doctor if:

- you have a history of epileptic seizures.
- you have recently experienced a myocardial infarction (heart attack), or if you are suffering from congestive heart failure or from an uncontrolled hypertension (high blood pressure).

In the above mentioned situations the treatment should be carefully supervised by the doctor, who will reassess the clinical benefit of Ebixa on a regular basis.

-you suffer from impaired function of the kidney (kidney problems), the doctor should closely monitor your kidney function and if necessary adapt the dosage accordingly.

If you are suffering from states of renal tubulary acidosis (RTA, an excess of acid-forming substances in the blood due to renal dysfunction (poor kidney function) or severe infections of the urinary tract (structure that carries urine), your doctor may need to adjust the dose of your medicine.

While using Ebixa, the use of the following medicinal products at the same time should be avoided:

- amantadine (for the treatment of Parkinson's disease),

- ketamine (a substance generally used as an anaesthetic),
- dextromethorphan (generally used to treat cough)
- other NMDA-antagonists

Children and adolescents
Ebixa is not recommended for children and adolescents under the age of 18 years.

Drug Interactions
If you are taking, or have recently taken, other medicines, including nonprescription medicines and nutritional supplements, tell the doctor or pharmacist. It is especially important to inform the doctor or pharmacist if you are taking the following medicines since Ebixa may change the effects of them and their dose may need to be adjusted by your doctor:

- amantadine, ketamine, dextromethorphan (see section " Special warnings regarding use of the medicine").
- dantrolene, baclofen
- cimetidine, ranitidine, procainamide, quinidine, quinine, nicotine
- hydrochlorothiazide (or any combination with hydrochlorothiazide)
- anticholinergics (substances generally used to treat movement disorders or intestinal cramps)
- medicines for the treatment of epilepsy (substances used to prevent and relieve seizures)
- barbiturates (substances generally used to induce sleep)
- dopaminergic agonists such as L-dopa, bromocriptine
- neuroleptics (used in the treatment of mental disorders)
- oral anticoagulants.

If you go into hospital, let your doctor know that you are taking Ebixa.

Use of the medicine and food
The medicine can be taken with or without food.
You should inform your doctor if you have recently changed or intend to change your diet substantially (e.g. from normal diet to strict vegetarian diet), as your doctor may need to adjust the dose of your medicine.

Pregnancy and breastfeeding
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 taking this medicine.

Pregnancy
The use of memantine in pregnant women is not recommended .

Breast-feeding
Women taking Ebixa should not breast-feed.

Driving and using machines
Your doctor will explain to you whether your illness allows you to drive and to use machines safely.
Also, Ebixa may change your reactivity, making driving or operating machinery inappropriate.

Important information about some of the ingredients of the medicine
This medicine contains sorbitol and potassium

This medicine contains 100 mg sorbitol in each gram which is equivalent to 200 mg /4 pump actuation. Sorbitol is a source of fructose. If your doctor told you that you have an intolerance to some sugars, or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you take or receive this medicine. Your doctor will advise you.

Furthermore, this medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially potassium-free.

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 about the dosage or the administration of the medicine.
The dosage and treatment regimen will be determined by the doctor only. The usual dosage is:

The recommended dose for adults and elderly patients is 20 mg (2 ml of solution) once daily.
In order to reduce the risk of side effects, this dose is achieved gradually by the following treatment scheme:

week 1	0.5 ml of solution (one pump actuation) per day
week 2	1 ml of solution (two pump actuations) per day
week 3	1.5 ml of solution (three pump actuations) per day
week 4 and beyond	2 ml of solution (four pump actuations) per day

The starting dose is 0.5 ml of solution (one pump actuation) per day during the first week.
In the second week – 1 ml of solution (two pump actuations) daily.
In the third week - 1.5 ml of solution (three pump actuations) daily.
From the fourth week and beyond – 2 ml of solution (four pump actuations) daily.
This medicine should be taken at the same time every day.

Dosage in patients with impaired kidney function:
In patients with mild impaired kidney function (Creatinine clearance 50-80 ml per minute), there is no need for dosage adjustment.
Dosage in patients with moderate impaired kidney function (Creatinine clearance 30-49 ml per minute), daily dosage is 10 mg (1 ml of solution, equivalent to two pump actuations). In case of tolerance to the medicine, after 7 days of treatment, dosage may be augmented to 20 mg daily.
Dosage in patients with severe impaired kidney function (Creatinine clearance 5-29 ml per minute), daily dosage is 10 mg (1 ml of solution, equivalent to two pump actuations).

Do not exceed the recommended dose.

Directions for use
The required dose should be put onto a spoon or into a glass with a little water using the pump and swallowed with a small amount of water.
The medicine can be taken with or without food.
The medicine should not be taken into the mouth directly from the bottle or the pump!
The attached pump should only be used for the Ebixa 5 mg/pump actuation oral solution bottle, and not for other products or containers.
After extracting the required measured dose, the pump should be locked.
After screwing the dosing pump onto the bottle when starting the use, it should never be unscrewed and the bottle should be kept standing vertically. See detailed instructions for use at the end of the leaflet.

If the pump does not function according to the instructions for use, consult your attending physician or a pharmacist.

- If you mistakenly took a higher dosage, contact the doctor or seek medical help. Taking an over dose will usually not result in any harm, but you may experience side effects (see section "side effects").
If a child swallowed the medicine by mistake, refer immediately to the physician or to a hospital emergency room and bring the package of the medicine with you.
- **If you have forgotten to take the medicine** at the specified time do not take a double dose.
Take the next dose at the usual time and consult the physician.
- This medicine should be taken at the specific time intervals determined by the attending doctor.
You should continue with the treatment as instructed by the doctor. Even if there is an improvement in your health, do not discontinue use of this medicine without consulting the doctor.

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

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

4. Side effects
As with all medicines, use of Ebixa 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. In general, the observed side effects are mild to moderate.

Common side effects (affects 1 to 10 users in 100):

Headache, sleepiness, constipation, elevated liver function tests, dizziness, balance disorders, shortness of breath, high blood pressure and allergic reaction to the drug (hypersensitivity).

Uncommon side effects (affects 1 to 10 users in 1,000):Tiredness, fungal infections, confusion, hallucinations, vomiting, abnormal gait, heart failure and venous blood clotting (thrombosis/thromboembolism).

Very rare side effects (affects less than 1 user in 10,000):
Seizures.

Side effects with unknown frequency (frequency cannot be estimated from the available data): Inflammation of the pancreas, inflammation of the liver (hepatitis) and psychotic reactions.

Alzheimer's disease has been associated with depression, suicidal ideation and suicide. These events have been reported in patients treated with Ebixa.

If you notice side effects, 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 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 a physician!
- 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.
The product can be used for 3 months after first opening the bottle.

- The bottle with the mounted pump must be kept and transported in an upright position only.
-Do not discard of medicines via wastewater or household waste. In order to protect the environment, consult the pharmacist how to dispose of medicines no longer required or expired.

6. ADDITIONAL INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
Purified water, Sorbitol 70% (non-crystallising), Potassium sorbate

- **What the medicine looks like and contents of the pack:** a clear, colourless to light yellowish solution.
Presented in a bottle.

- Registration Holder: Lundbeck Israel Ltd., 11 Galgaley Haplada, P.O.B. 13105, Herzliya 4672211.
Fax: 03- 9100116, email address: Israel@lundbeck.com.

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

- Revised in May 2021 according to MoH guidelines.

- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:**
140 63 30890

Instruction for proper use of the pump :

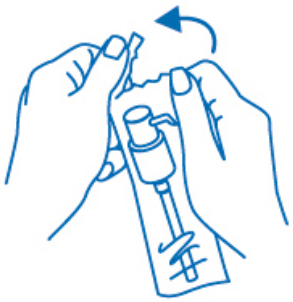
1. Prior to the first use the screw cap should be completely removed from the bottle by turning it anticlockwise (drawing 1).

1.

Mounting the dosing pump on the bottle:

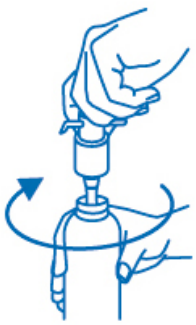
2.The pump should be removed from the bag attached to the product's package (drawing 2) and the plastic tube should be inserted carefully into the bottle.

2.



3.The pump should be held onto the neck of the bottle and screwed clockwise until it is attached (drawing 3). The pump should be screwed once when starting the use, and should not be removed from the bottle after that.

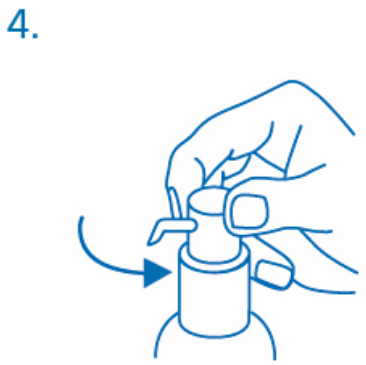
3.



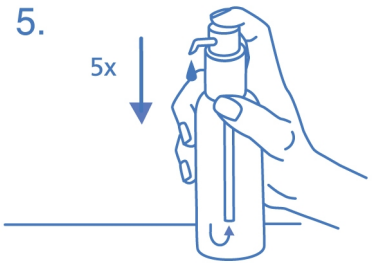
Using the pump for extracting measured doses:

The dosing pump head has two positions and is easy to turn:
-anticlockwise to unlock and
-clockwise to lock.

4.
The dosing pump head should not be pushed down while in the locked position. The solution may only be dispensed in the unlocked position. To unlock, turn the pump head (in the direction of the arrow, drawing 4) until it cannot be turned any further. The dosing pump is then ready for use.



5. **Preparing the dosing pump:** Before taking a measured dose for the first time, the pump should be prepared for use by pushing the pump down completely five times in succession (drawing 5). Any solution that is extracted during this action should not be used because at this stage the extracted solution does not contain a measured and correct dose of the medicine.



6. After completing the required action in section 5, each downward stroke of the pump will extract a measured dose of 0.5 ml solution that contains 5 mg of the active ingredient Memantine Hydrochloride (drawing 6).

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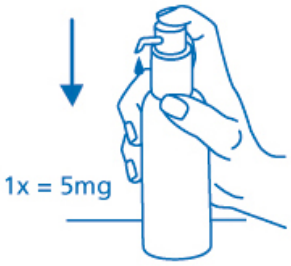

7. **Correct use of the pump:** the bottle should be placed on a flat, horizontal surface, such as a table and be used only when it is standing vertically. A glass with a little water or a spoon should be held below the nozzle and the pump should be pushed down (not too slowly) right down to a stop (drawings 7 and 8). Thereafter, the pump can be released and pushed down again in order to extract another measured dose.

7.

8.