Patient leaflet in accordance with Pharmacist's Regulations (Preparations) 1986

The medicine is marketed according to doctor's prescription only.

Brintellix, coated tablets

5 mg, 10 mg, 15 mg, 20 mg

Composition: the active ingredient and its quantity:

Brintellix 5 mg: Each coated tablet contains 5 mg Vortioxetine (as hydrobromide)

Brintellix 10 mg: Each coated tablet contains 10 mg Vortioxetine (as hydrobromide)

Brintellix 15 mg: Each coated tablet contains 15 mg Vortioxetine (as hydrobromide)

Brintellix 20 mg: Each coated tablet contains 20 mg Vortioxetine (as hydrobromide)

Inactive ingredients: See section 6

- **Read this leaflet carefully in its entirety before using this medicine.** This leaflet contains essential information about this medicine. If you have any further question, consult your doctor or pharmacist.
- This medicine was 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 your own.

1. What is the medicine being used for?

Brintellix belongs to a group of medicines called antidepressants and you have been given this medicine to treat your depression.

Brintellix is used to treat major depressive episodes in adults.

Brintellix has been shown to reduce the broad range of depressive symptoms, including sadness, inner tension (feeling anxious), sleep disturbances, reduced appetite, difficulty in concentrating, feelings of worthlessness, loss of interest in favourite activities, feeling of being slowed down.

2. Before using this medicine

Do not take this medicine if:

-You are sensitive (allergic) to the active ingredient or any of the other ingredients of this medicine (listed in section 6).

- if you are taking other medicines for depression known as non-selective monoamine oxidase inhibitors or selective MAO-A inhibitors. Ask your doctor if you are uncertain.

Warnings and precautions

Before using Brintellix, tell your doctor if you:

- are taking medicines with a so-called serotonergic effect, such as:

  - tramadol and similar medicines (strong painkillers)

  - sumatriptan and similar medicines with active substance names ending in "triptans" (used to treat migraine)

Taking these medicines together with Brintellix may increase the risk of **serotonin syndrome**. This syndrome may be associated with hallucinations, involuntary twitching, accelerated heartbeat, high blood pressure, fever, nausea and diarrhoea.

- have had fits (seizures).

Your doctor will treat you cautiously if you have a history of fits or have unstable fit disorders/epilepsy. Fits are a potential risk with medicines used to treat depression. Treatment should be discontinued in any patient who develops fits or where there is an increase in the frequency of fits.

- have had mania

- have a tendency to bleed or bruise easily, or if you are pregnant (See 'Pregnancy, breast-feeding and fertility').

- have low sodium level in the blood.

- are 65 years of age or older.

- have a severe kidney disease.

- have a severe liver disease or a liver disease called cirrhosis.

- have or previously have had increased pressure in the eye or glaucoma. If your eyes become painful and you develop blurred vision during treatment, contact your doctor.

When you are on antidepressant treatment, including vortioxetine, you may also experience feelings of aggression, agitation, anger and irritability. If this occurs, you should talk to your doctor.

Thoughts of suicide and worsening of your depression

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.

- are a young adult.

Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years 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

Brintellix is not recommended in children and adolescents under 18 years due to lack of information for this age group.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and dietary supplements, inform your doctor or pharmacist. This is especially important if you are taking:

-phenelzine, iproniazid, isocarboxazid, nialamide, tranylcypromine (medicines to treat depression called non-selective monoamine oxidase inhibitors) you must not take any of these medicines together with Brintellix.

If you have taken any of these medicines, you will need to wait 14 days before you start taking Brintellix.

After stopping Brintellix, you must allow 14 days before taking any of these medicines.

- moclobemide (a medicine to treat depression).

- selegiline, rasagiline (medicines to treat Parkinson's disease).

- linezolid (a medicine to treat bacterial infections).

- medicinal products with serotonergic effect e.g. tramadol and similar medicines (strong painkillers) and sumatriptan and similar medicines with active substance names ending in "triptans" (used to treat migraine). Taking these medicines together with Brintellix may increase the risk of serotonin syndrome (see section warnings and precautions).

- lithium (a medicine to treat depression and mental disorders) or tryptophan.

- medicines known to cause low sodium level.

- rifampicin (a medicine to treat tuberculosis and other infections).

- carbamazepine, phenytoin (medicines to treat epilepsy or other illness).

- warfarin, dipyridamole, phenprocoumon, low-dose acetylsalicylic acid (aspirin) (blood thinning medicines).

Medicines that increase the risk of epileptic fits:

-sumatriptan and similar medicines with active substance names ending in “triptans.”

-tramadol (a strong painkiller).

-mefloquine (a medicine to prevent and treat malaria).

-bupropion (a medicine to treat depression also used to wean from smoking).

-fluoxetine, paroxetine and other medicines to treat depression called SSRI/SNRIs, tricyclics.

-St John’s wort (hypericum perforatum) (a medicine to treat depression).

-quinidine (a medicine to treat heart rhythm disorders)

-chlorpromazine, chlorprothixene, haloperidol (medicines to treat mental disorders belonging to the groups called phenothiazines, thioxanthenes, butyrophenones).

Please tell your doctor if you are taking any of the medicines above, since your doctor needs to know if you already are at risk for siezures.

If you are having a urine drug screen, taking Brintellix may cause positive results for methadone when some test methods are used, even though you may not be taking methadone. If this happens, a more specific test can be performed.

This medicine use and food

You can take this medicine with or without food.

This medicine and alcohol consumption

Combining this medicine with alcohol is not advisable.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Pregnancy

Brintellix should not be used during pregnancy unless the doctor says it is absolutely necessary.

If you take medicines to treat depression, including Brintellix, during the last 3 months of your pregnancy, you should be aware that the following effects may be seen in your newborn baby: trouble with breathing, bluish skin, fits, body temperature changes, feeding difficulties, vomiting, low blood sugar, stiff or floppy muscles, vivid

reflexes, tremor, jitteriness, irritability, lethargy, constant crying, sleepiness and sleeping difficulties.

Contact your doctor immediately if your newborn baby has any of these symptoms.

Make sure your midwife and/or doctor know you are on Brintellix. When taken during pregnancy, particularly in the last 3 months of pregnancy, medicines like Brintellix 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.

If you take Brintellix 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 Brintellix so they can advise you.

Breast-feeding

It is expected that the ingredients of Brintellix will pass into breast milk. Brintellix is not to be used during breast-feeding. Your doctor will make a decision on whether you should stop breast-feeding, or stop using Brintellix taking into account the benefit of breast-feeding for your child, and the benefit of therapy for you.

Driving and using machines

Brintellix has no or negligible influence on the ability to drive and use machines. However, as adverse reactions such as dizziness have been reported, caution is advised during such activities when beginning Brintellix treatment or changing the dose.

Brintellix contains Sodium

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

3. How to take this medicine?

Always use according to the doctor's instructions**.** Check with your doctor or pharmacist if you are not sure. Dosage is according to doctor's instructions only. The usual recommended dose is:

10 mg taken as one daily dose in adults less than 65 years of age. The dose may be increased by your doctor to a maximum of 20 mg per day or lowered to a minimum of 5 mg per day depending on your response to treatment.

For elderly people 65 years of age or older, the starting dose is 5 mg vortioxetine taken once daily.

Do not exceed the recommended dose.

Take one tablet with a glass of water. The tablet can be taken with or without food.

There is no information regarding the cutting or the crushing of the tablets.

Duration of treatment:

Take Brintellix for as long as your doctor recommends.

Continue to take Brintellix even if it takes some time before you feel any improvement in your condition.

Treatment should be continued until your doctor tells you to stop.

If you have taken an overdose or if a child accidently swallowed some of the medicine contact your doctor or nearest hospital emergency department immediately and bring the container and any remaining tablets with you. Do this even if you do not feel any effect or signs of discomfort. Overdose signs are dizziness, nausea, diarrhea, stomach discomfort, itching of the whole body, sleepiness and flushing.

Following intake of dosages several times higher than the prescribed dose, fits (seizures) and a rare condition called serotonin syndrome have been reported.

If you forget to take this medicine at the correct time

Take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose**.**

The treatment should be continued as recommended by the doctor.

If you stop taking the medicine

Even if your health condition has improved, do not stop taking Brintellix without consulting with your doctor.

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

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

4. **<u>Side effects</u>**:

Like all medicines, Brintellix can cause side effects in some of the patients. Do not be alarmed by the list of side effects. You might not experience any of them.

In general, the observed side effects were mild to moderate and occurred within the first two weeks of treatment. The reactions were usually temporary and did not lead to cessation of therapy.

Side effects listed below have been reported in the following frequencies:

Very common: may affect more than 1 in 10 people

- nausea

Common: may affect 1-10 patients in 100

- diarrhea, constipation, vomiting

- dizziness

- itching of the whole body

- abnormal dreams

- increased sweating

Uncommon: may affect 1-10 patients in 1,000

- flushing

- night sweats

Rare: may affect 1-10 patients in 10000

- enlarged pupils (mydriasis), which can increase the risk of glaucoma (see section 2)

Not known: frequency cannot be estimated from available data

- low levels of sodium in the blood (the symptoms may include feeling dizzy, weak, confused, sleepy or very tired, or feeling or being sick; more serious symptoms are fainting, fits or falls)

- serotonin syndrome (see section 2)

- allergic reactions, that may be serious, causing swelling of the face, lips, tongue or throat, difficulties breathing or swallowing, and/or a sudden drop in blood pressure (making you feel dizzy or lightheaded)

- hives
- excessive or unexplained bleeding (including bruising, nose bleeding, gastrointestinal and vaginal bleeding)
- rash
- sleep disorders (insomnia)
- agitation and aggression. If you experience these side effects, contact your doctor (see section 2).
- headache
- increase in a hormon called prolactin in the blood

An increased risk of bone fractures has been observed in patients taking this type of medicine.

If you get any of the above mentioned side effects, if any of the side effects is worsening, or if you notice any side effect not listed in this leaflet, you should consult with your 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 the following link:

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

5. How to store the medicine?

Avoid poisoning! This medicine and all other medicines must be stored in a safe place out of the sight and reach of children and/ or infants, to avoid poisoning.

Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Storage conditions: Do not store in temperature exceeding 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. Other information

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

mannitol (E421), microcystalline cellulose, hydroxypropylcellulose, sodium starch glycolate (type A), magnesium stearate, hypromellose, Macrogol 400 **5 mg:** titanium dioxide (E171), iron oxide red (E172), **10 mg:** titanium dioxide (E 171), iron oxide yellow (E 172), **15 mg:** titanium dioxide (E171), iron oxide red (E172), iron oxide yellow (E 172), **20 mg:** titanium dioxide (E171), iron oxide red (E172).

What the medicine looks like and contents of the pack:

5 mg: Pink, almond-shaped 5 x 8.4 mm film-coated tablet marked with "TL" on one side and "5" on the other side**.**

10 mg: Yellow, almond-shaped 5 x 8.4 mm film-coated tablet marked with "TL" on one side and "10" on the other side.

15 mg: Orange, almond-shaped 5 x 8.4 mm film-coated tablet marked with "TL" on one side and "15" on the other side.

20 mg: Red, almond-shaped 5 x 8.4 mm film-coated tablet marked with "TL" on one side and "20" on the other side.

The tablets are in blister pack of 7, 14 and 28 tablets. Not all pack sizes may be marketed.

Registration holder name and address :

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

E-Mail: Israel@lundbeck.com

The manufacturer name and address: H. Lundbeck A/S, Ottiliavej 9, DK-2500 Valby, Denmark

Revised in 14 October 2021 according to MoH's guidelines.

Registration number of the medicine in the ministry of health registry:

Brintellix 5 mg: 153 72 34152

Brintellix 10 mg: 153 73 34155

Brintellix 15 mg: 153 74 34156

Brintellix 20 mg: 153 75 34157