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

This medicine is dispensed with a doctor's prescription only

Brintellix
5 mg, 10 mg, 15 mg, 20 mg
Film-coated tablets

Active ingredient
Brintellix 5 mg: Each film-coated tablet contains 5 mg *vortioxetine (as hydrobromide)*
Brintellix 10 mg: Each film-coated tablet contains 10 mg *vortioxetine (as hydrobromide)*
Brintellix 15 mg: Each film-coated tablet contains 15 mg *vortioxetine (as hydrobromide)*
Brintellix 20 mg: Each film-coated tablet contains 20 mg *vortioxetine (as hydrobromide)*

Inactive ingredients in this medicine: See 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 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 to yours.

Antidepressants increase the risk of suicidal behaviour and thoughts in children, adolescents, and young adults.

Upon starting treatment with the medicine, patients of all ages and their relatives must monitor behavioural changes such as worsening depression, suicidal thoughts, and aggression. If such changes occur, you should contact your doctor immediately.

1. What is this medicine intended for?

Brintellix is used to treat major depressive episodes in adults.
Therapeutic group: antidepressants.

Brintellix has been shown to reduce a 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 to any of the other ingredients in this medicine (see list of inactive ingredients in section 6).
- You are taking other medicines for depression known as non-selective monoamine oxidase (MAO) inhibitors or selective MAO-A inhibitors. Ask your doctor if you are uncertain.

Special warnings about using this medicine

Before using Brintellix, tell your doctor if:

- You are taking medicines with a serotonergic effect, such as:
  - tramadol and similar medicines (strong painkillers)

- sumatriptan and similar medicines with active substance names ending in “triptan” (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.
- You have had fits (seizures).
  Your doctor will treat you cautiously if you have a history of fits or have a fit disorder or unstable 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.
- you have had mania
- you have a tendency to bleed or bruise easily, or if you are pregnant (see ‘Pregnancy, breast-feeding, and fertility’)
- you have low sodium level in the blood
- you are 65 years of age or older
- you have a severe kidney disease
- you have a severe liver disease or a liver disease called cirrhosis
- you have ever 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 tell 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 take time to work, usually about two weeks but sometimes longer.

You may be more likely to have such thoughts:
- 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 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 advisable 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 for use in children and adolescents under 18 years of age.

Interactions with other medicines
If you are taking or have recently taken other medicines, including non-prescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly 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 (to treat depression)
- selegiline, rasagiline (to treat Parkinson's disease)
- linezolid (to treat bacterial infections)
- medicinal products with a serotonergic effect such as tramadol and similar medicines (strong painkillers), and sumatriptan and similar medicines with active substance names ending in "triptan" (used to treat migraine). Taking these medicines together with Brintellix may increase the risk of serotonin syndrome (see under 'Special warnings about using this medicine').
- lithium (to treat depression and mental disorders) or tryptophan
- medicines known to cause low sodium level
- rifampicin (to treat tuberculosis and other infections).
- carbamazepine, phenytoin (to treat epilepsy or other illnesses)
- warfarin, dipyridamole, phenprocoumon, some antipsychotics, phenothiazines, tricyclic antidepressants, low-dose acetylsalicylic acid (aspirin) and non-steroidal anti-inflammatory drugs (blood thinning medicines and medicines used for pain relief). These may increase bleeding-tendency.

Medicines that increase the risk of epileptic fits (seizures)**:**

- sumatriptan and similar medicines with active substance names ending in "triptan"
- tramadol (a strong painkiller)
- mefloquine (to prevent and treat malaria)
- bupropion (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) (to treat depression)
- quinidine (to treat heart rhythm disorders)
- chlorpromazine, chlorprothixene, haloperidol (medicines to treat mental disorders, which belong 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 seizures.

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.

Using this medicine and food
You can take this medicine with or without food.

Using 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.

<u>Pregnancy</u>
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 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 decide 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 side effects such as dizziness have been reported, caution is advised during such activities when beginning Brintellix treatment or changing the dose.

Important information about some of this medicine's ingredients
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 this medicine according to the 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. The recommended dosage is usually:
10 mg once daily 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 taken once daily.

Do not exceed the recommended dose.
Take one tablet with a glass of water. The medicine can be taken with or without food.
There is no information about crushing or splitting 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 accidentally taken an overdose or if a child has accidently swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package and remaining tablets with you. Do this even if you do not feel any effect or signs of discomfort. Overdose signs could be dizziness, nausea, diarrhoea, stomach discomfort, itching all over, sleepiness, and flushing.

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

If you forget to take this medicine at the scheduled time, take the next dose at the usual time. Do not take a double dose to make up for the dose you forgot.

Adhere to the treatment as recommended by your doctor.

If you stop taking the medicine
Even if your health improves, do not stop taking this medicine without consulting your doctor. Your doctor may decide to reduce your dose before you finally stop taking this medicine.

Some patients who stop taking Brintellix have experienced symptoms such as dizziness, headache, tingling feelings like pins and needles or electric shock-like feelings (particularly in the head), inability to sleep, nausea or vomiting, feeling anxious, irritable or agitated, feeling tired or shaking. These symptoms may occur within the first week after stopping Brintellix.

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, ask your doctor or pharmacist.

4. <u>Side effects</u>

As with any medicine, using Brintellix can cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.
In general, the observed side effects were mild to moderate and occurred during 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 side effects: may affect more than 1 in 10 users

- nausea

Common side effects: may affect 1–10 in 100 users

- diarrhoea
- constipation
- vomiting
- dizziness
- itching of the whole body, itching
- abnormal dreams
- increased sweating
- indigestion

Uncommon side effects: may affect 1–10 in 1,000 users

- flushing
- night sweats
- blurred vision
- involuntary shaking (tremor)
- hallucinations (seeing, hearing, or feeling things that are not there)

Rare side effects: may affect 1–10 in 10,000 users

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

Side effects of unknown frequency (frequency not established yet)

- low levels of sodium in the blood (the symptoms may include feeling dizzy, weak, confused, sleepy or very tired, nausea or vomiting; 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 (rash)
- 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 the hormone prolactin in the blood
- a constant and uncontrollable urge to move (akathisia)
- grinding one's teeth (bruxism)
- inability to open your mouth (lockjaw/trismus)
- restless leg syndrome (urges to move the legs to stop painful or odd sensations, often occurring at night)
- abnormal milky discharge from the breast (galactorrhoea)
- withdrawal syndrome.

An increased risk of bone fractures has been observed in patients taking this type of medicine.
An increased risk of sexual dysfunction has been reported with the 20 mg dose, and in some patients this side effect was observed at lower doses.

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.

Reporting of side effects
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: Store below 30°C.

Do not throw away medicines via household waste or wastewater. Ask the 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:
mannitol, cellulose microcystalline, hydroxypropylcellulose (5%, 75%-150 mPa.s), sodium starch glycolate (type A), magnesium stearate, hypromellose (6 mPa.s), macrogol 400, water purified
5 mg: titanium dioxide, iron oxide red; **10 mg**: titanium dioxide, iron oxide yellow; **15 mg:** titanium dioxide, iron oxide red, iron oxide yellow; **20 mg:** titanium dioxide, iron oxide red.

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 packs of 7, 14, or 28 tablets.
Not all pack sizes may be marketed.

Registration holder’s name and address:
Lundbeck Israel Ltd., 11 Galgaley Haplada, P.O.B. 13105, Herzliya 4672211

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

Revised in November 2025.

Registration number of the medicine in the Ministry of Health’s National Drug 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