



Brintellix® film-coated tablets
Vortioxetine (as hydrobromide)

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

See full prescribing information for complete boxed warning.

- Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants (5.1).
- Monitor for worsening and emergence of suicidal thoughts and behaviors (5.1).
- BRINTELLIX has not been evaluated for use in pediatric patients (8.4).

1. NAME OF THE MEDICINAL PRODUCT

Brintellix 5 mg film-coated tablets
Brintellix 10 mg film-coated tablets
Brintellix 20 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Brintellix 5 mg film-coated tablets

Each film-coated tablet contains vortioxetine hydrobromide equivalent to 5 mg vortioxetine.

Brintellix 10 mg film-coated tablets

Each film-coated tablet contains vortioxetine hydrobromide equivalent to 10 mg vortioxetine.

Brintellix 20 mg film-coated tablets

Each film-coated tablet contains vortioxetine hydrobromide equivalent to 20 mg vortioxetine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Brintellix 5 mg film-coated tablets

Pink, almond-shaped (5 x 8.4 mm) film-coated tablet engraved with “TL” on one side and “5” on the other side.

Brintellix 10 mg film-coated tablets

Yellow, almond-shaped (5 x 8.4 mm) film-coated tablet engraved with “TL” on one side and “10” on the other side.

Brintellix 20 mg film-coated tablets

Red, almond-shaped (5 x 8.4 mm) film-coated tablet engraved with “TL” on one side and “20” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Brintellix is indicated for the treatment of major depressive disorder in adults. The efficacy of Brintellix was demonstrated in 6 to 8 week studies (including one study in the elderly).

4.2 Posology and method of administration

Posology (tablet)

The starting and recommended dose of Brintellix is 10 mg vortioxetine once daily in adults less than 65 years of age.

Depending on individual patient response, the dose may be increased to a maximum of 20 mg vortioxetine once daily or decreased to a minimum of 5 mg vortioxetine once daily.

Treatment discontinuation

Patients treated with vortioxetine can abruptly stop taking the medicinal product without the need for a gradual reduction in dose (see section 5.1).

Special population

Elderly patients

The lowest effective dose of 5 mg vortioxetine once daily should always be used as the starting dose in patients ≥ 65 years of age. Caution is advised when treating patients ≥ 65

years of age with doses higher than 10 mg vortioxetine once daily for which data are limited (see section 4.4).

Method of administration

Brintellix is for oral use.

The film-coated tablets can be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Concomitant use with non-selective monoamine oxidase inhibitors (MAOIs) or selective MAO-A inhibitors (see section 4.5).

4.4 Special warnings and precautions for use

Use in paediatric population

Brintellix is not recommended for the treatment of depression in patients aged less than 18 years since the safety and efficacy of vortioxetine have not been established in this age group (see section 4.2). In clinical studies in children and adolescents treated with other antidepressants, suicide-related behaviour (suicide attempt and suicidal thoughts) and hostility (predominantly aggression, oppositional behaviour, anger) were more frequently observed than in those treated with placebo.

Suicide/suicidal thoughts or clinical worsening

Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Patients with a history of suicide-related events or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical studies of antidepressants in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo, in patients less than 25 years old.

Close supervision of patients and in particular those at high risk should accompany treatment especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted to the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Seizures

Seizures are a potential risk with antidepressants. Therefore, vortioxetine should be introduced cautiously in patients who have a history of seizures or in patients with unstable epilepsy (see section 4.5). Treatment should be discontinued in any patient who develops seizures or for whom there is an increase in seizures frequency.

Serotonin Syndrome (SS) or Neuroleptic Malignant Syndrome (NMS)

Serotonin Syndrome (SS) or Neuroleptic Malignant Syndrome (NMS), potentially life-threatening conditions, may occur with vortioxetine. The risk of SS or NMS is increased with concomitant use of serotonergic-active substances (including triptans), antipsychotics, and other dopamine antagonists. Patients should be monitored for the emergence of signs and symptoms of SS or NMS (see sections 4.3 and 4.5).

Serotonin Syndrome symptoms include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, uncoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea). If this occurs, treatment with vortioxetine should be discontinued immediately and symptomatic treatment should be initiated.

Mania/hypomania

Vortioxetine should be used with caution in patients with a history of mania/hypomania and should be discontinued in any patient entering a manic phase.

Aggression/agitation

Patients treated with antidepressants, including vortioxetine, may also experience feelings of aggression, anger, agitation and irritability. Patient's condition and disease status should be closely monitored. Patients (and caregivers of patients) should be alerted to seek medical advice, if aggressive/agitated behaviour emerges or aggravates.

Haemorrhage

Bleeding abnormalities, such as ecchymoses, purpura and other haemorrhagic events, such as gastrointestinal or gynaecological bleeding, have been reported rarely with the use of antidepressants with serotonergic effect Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs). Caution is advised in patients taking anticoagulants and/or medicinal products known to affect platelet function [e.g., atypical antipsychotics and phenothiazines, most tricyclic antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (ASA)] (see section 4.5) and in patients with known bleeding tendencies/disorders.

Hyponatremia

Hyponatraemia, probably due to inappropriate antidiuretic hormone secretion (SIADH), has been reported rarely with the use of antidepressants with serotonergic effect (SSRIs, SNRIs). Caution should be exercised in patients at risk, such as the elderly, patients with cirrhosis of the liver or patients concomitantly treated with medicinal products known to cause hyponatremia.

Discontinuation of vortioxetine should be considered in patients with symptomatic hyponatraemia and appropriate medical intervention should be instituted.

Glaucoma

Mydriasis has been reported in association with use of antidepressants, including vortioxetine. This mydriatic effect has the potential to narrow the eye angle resulting in increased intraocular pressure and angle-closure glaucoma. Caution is advised when prescribing vortioxetine to patients with increased intraocular pressure, or those at risk of acute narrow-angle glaucoma.

Elderly

Data on the use of Brintellix in elderly patients with major depressive episodes are limited. Therefore, caution should be exercised when treating patients ≥ 65 years of age with doses higher than 10 mg vortioxetine once daily (see sections 4.2, 4.8 and 5.2).

Brintellix contains Sodium

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

4.5 Interaction with other medicinal products and other forms of interaction

Vortioxetine is extensively metabolised in the liver, primarily through oxidation catalysed by CYP2D6 and to a minor extent CYP3A4/5 and CYP2C9 (see section 5.2).

Potential for other medicinal products to affect vortioxetine

Irreversible non-selective MAOIs

Due to the risk of serotonin syndrome, vortioxetine is contraindicated in any combination with irreversible non-selective MAOIs. Vortioxetine must not be initiated for at least 14 days after discontinuation of treatment with an irreversible non-selective MAOI. Vortioxetine must be discontinued for at least 14 days before starting treatment with an irreversible non-selective MAOI (see section 4.3).

Reversible, selective MAO-A inhibitor (moclobemide)

The combination of vortioxetine with a reversible and selective MAO-A inhibitor, such as moclobemide, is contraindicated (see section 4.3). If the combination proves necessary, the added medicinal product should be given with minimum dosage and under close clinical monitoring for serotonin syndrome (see section 4.4).

Reversible, non-selective MAOI (linezolid)

The combination of vortioxetine with a weak reversible and non-selective MAOI, such as the antibiotic linezolid, is contraindicated (see section 4.3). If the combination proves necessary, the added medicinal product should be given with minimum dosage and under close clinical monitoring for serotonin syndrome (see section 4.4).

Irreversible, selective MAO-B inhibitor (selegiline, rasagiline)

Although a lower risk of serotonin syndrome is expected with selective MAO-B inhibitors than with MAO-A inhibitors, the combination of vortioxetine with

irreversible MAO-B inhibitors, such as selegiline or rasagiline should be exercised with caution. Close monitoring for serotonin syndrome is necessary if used concomitantly (see section 4.4).

Serotonergic medicinal products

Co-administration of medicinal products with serotonergic effect (e.g., tramadol, sumatriptan and other triptans) may lead to serotonin syndrome (see section 4.4).

St. John's wort

Concomitant use of antidepressants with serotonergic effect and herbal remedies containing St. John's wort (*Hypericum perforatum*) may result in a higher incidence of adverse reactions including Serotonin Syndrome (see section 4.4).

Medicinal products lowering the seizure threshold

Antidepressants with serotonergic effect can lower the seizure threshold. Caution is advised when concomitantly using other medicinal products capable of lowering the seizure threshold [e.g., antidepressants (tricyclics, SSRIs, SNRIs), neuroleptics (phenothiazines, thioxanthenes and butyrophenones), mefloquine, bupropion, tramadol] (see section 4.4).

ECT (electroconvulsive therapy)

There is no clinical experience with concurrent administration of vortioxetine and ECT, therefore caution is advisable.

CYP2D6 inhibitors

The exposure to vortioxetine increased 2.3-fold for area under the curve (AUC) when vortioxetine 10 mg/day was co-administered with bupropion (a strong CYP2D6 inhibitor 150 mg twice daily) for 14 days in healthy subjects. Co-administration resulted in a higher incidence of adverse reactions when bupropion was added to vortioxetine than when vortioxetine was added to bupropion. Depending on individual patient response, a lower dose of vortioxetine may be considered if strong CYP2D6 inhibitor (e.g., bupropion, quinidine, fluoxetine, paroxetine) is added to vortioxetine treatment (see section 4.2).

CYP3A4 inhibitors and CYP2C9, and CYP2C19 inhibitors

When vortioxetine was co-administered following 6 days of ketoconazole 400 mg/day (a CYP3A4/5 and P-glycoprotein inhibitor) or following 6 days of fluconazole 200 mg/day (a CYP2C9, CYP2C19, and CYP3A4/5 inhibitor) in healthy subjects, a 1.3-fold and 1.5-fold increase, respectively, in vortioxetine AUC was observed. No dose adjustment is needed.

No inhibitory effect of 40 mg single-dose omeprazole (CYP2C19 inhibitor) was observed on the multiple-dose pharmacokinetics of vortioxetine in healthy subjects.

Interactions in CYP2D6 poor metabolisers

Co-administration of strong inhibitors of CYP3A4 (such as itraconazole, voriconazole, clarithromycin, telithromycin, nefazodone, conivaptan and many of the HIV protease inhibitors) and inhibitors of CYP2C9 (such as fluconazole and amiodarone) to CYP2D6 poor metabolisers (see section 5.2) has not been investigated specifically, but it is anticipated that it will lead to a more marked increased exposure of vortioxetine in these patients as compared to the moderate effect described above.

Depending on individual patient response, a lower dose of vortioxetine may be considered if a strong inhibitor of CYP3A4 or CYP2C9 is co-administered in CYP2D6 poor metabolisers.

Cytochrome P450 inducers

When a single dose of 20 mg vortioxetine was co-administered following 10 days of rifampicin 600 mg/day (a broad inducer of CYP isozymes) in healthy subjects, a 72% decrease in AUC of vortioxetine was observed. Depending on individual patient response, a dose adjustment may be considered if a broad cytochrome P450 inducer (e.g., rifampicin, carbamazepine, phenytoin) is added to vortioxetine treatment (see section 4.2).

Alcohol

No effect on the pharmacokinetics of vortioxetine or ethanol and no significant impairment, relative to placebo, in cognitive function were observed when vortioxetine in a single dose of 20 mg or 40 mg was co-administered with a single dose of ethanol (0.6 g/kg) in healthy subjects. However, alcohol intake is not advisable during antidepressant treatment.

Acetylsalicylic acid

No effect of multiple doses of acetylsalicylic acid 150 mg/day on the multiple-dose pharmacokinetics of vortioxetine was observed in healthy subjects.

Potential for vortioxetine to affect other medicinal products

Anticoagulants and antiplatelet medicinal products

No significant effects, relative to placebo, were observed in INR, prothrombin or plasma R-/S-warfarin values following co-administration of multiple doses of vortioxetine with stable doses of warfarin in healthy subjects. Also, no significant inhibitory effect, relative to placebo, on platelet aggregation or pharmacokinetics of acetylsalicylic acid or salicylic acid was observed when acetylsalicylic acid 150 mg/day was co-administered following multiple doses of vortioxetine administration in healthy subjects. However, caution should be exercised when vortioxetine is combined with oral anticoagulants or antiplatelet medicinal products due to a potential increased risk of bleeding attributable to a pharmacodynamic interaction (see section 4.4).

Cytochrome P450 substrates

In vitro, vortioxetine did not show any relevant potential for inhibition or induction of cytochrome P450 isozymes (see section 5.2).

Following multiple doses of vortioxetine, no inhibitory effect was observed in healthy subjects for the cytochrome P450 isozymes CYP2C19 (omeprazole, diazepam), CYP3A4/5 (ethinyl estradiol, midazolam), CYP2B6 (bupropion), CYP2C9 (tolbutamide, S-warfarin), CYP1A2 (caffeine) or CYP2D6 (dextromethorphan).

No pharmacodynamic interactions were observed. No significant impairment, relative to placebo, in cognitive function was observed for vortioxetine following co-administration with a single 10 mg dose of diazepam. No significant effects, relative to placebo, were observed in the levels of sex hormones following co-administration of vortioxetine with a combined oral contraceptive (ethinyl estradiol 30 µg/levonorgestrel 150 µg).

Lithium, tryptophan

No clinically relevant effect was observed during steady-state lithium exposure following co-administration with multiple doses of vortioxetine in healthy subjects. However, there have been reports of enhanced effects when antidepressants with serotonergic effect have been given together with lithium or tryptophan, therefore, concomitant use of vortioxetine with these medicinal products should be undertaken with caution.

Interference with urine drug screens

There have been reports of false positive results in urine enzyme immunoassays for methadone in patients who have taken vortioxetine. Caution should be exercised in the interpretation of positive urine drug screen results, and confirmation by an alternative analytical technique (e.g., chromatographic methods) should be considered.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of vortioxetine in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3).

The following symptoms may occur in the newborn after maternal use of a serotonergic medicinal product in the later stages of pregnancy: respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty sleeping. These symptoms could be due to either discontinuation effects or excess serotonergic activity. In the majority of instances, such complications began immediately or soon (<24 hours) after delivery.

Epidemiological data suggest that the use of SSRIs in pregnancy, particularly in late pregnancy, may increase the risk of persistent pulmonary hypertension in the newborn (PPHN). Although no studies have investigated the association of PPHN with vortioxetine treatment, this potential risk cannot be ruled out taking into account the related mechanism of action (increase in serotonin concentrations).

Brintellix should only be administered to pregnant woman if the expected benefits outweigh the potential risk to the foetus.

Breast-feeding

Available data in animals have shown excretion of vortioxetine/ vortioxetine metabolites in milk. It is expected that vortioxetine will be excreted into human milk (see section 5.3).

A risk to the breastfeeding child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Brintellix treatment taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

Fertility studies in male and female rats showed no effect of vortioxetine on fertility, sperm quality or mating performance (see section 5.3).

Human case reports with medicinal products from the related pharmacological class of antidepressants (SSRIs) have shown an effect on sperm quality that is reversible. Impact on human fertility has not been observed so far.

4.7 Effects on ability to drive and use 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, patients should exercise caution when driving or operating hazardous machinery, especially when starting treatment with vortioxetine or when changing the dose.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reaction was nausea.

Tabulated list of adverse reactions

Adverse reactions are listed below using the following convention: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data). The list is based on information from clinical trials and post-marketing experience.

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTION
Immune system disorders	Not known*	Anaphylactic reaction
Metabolism and nutrition disorders	Not known*	Hyponatremia
Psychiatric disorders	Common	Abnormal dreams
	Not known*	Insomnia
	Not known*	Agitation, aggression (see section 4.4)
Nervous system disorders	Common	Dizziness
	Not known*	Serotonin Syndrome
Eye disorders	Rare	Mydriasis (which may lead to acute narrow angle glaucoma see section 4.4)
Vascular disorders	Uncommon	Flushing
	Not known*	Haemorrhage (including contusion,

		ecchymosis, epistaxis, gastrointestinal or vaginal bleeding)
Gastrointestinal disorders	Very common	Nausea
	Common	Diarrhoea, Constipation, Vomiting
Skin and subcutaneous tissue disorders	Common	Pruritus, including pruritus generalised
	Uncommon	Night sweats
	Not known*	Angioedema, Urticaria, Rash

*Based on post-marketing cases

Description of selected adverse reactions

Nausea

Nausea was usually mild or moderate and occurred within the first two weeks of treatment. The reactions were usually transient and did not generally lead to cessation of therapy. Gastrointestinal adverse reactions, such as nausea, occurred more frequently in women than men.

Elderly patients

For doses ≥ 10 mg vortioxetine once daily, the withdrawal rate from the studies was higher in patients aged ≥ 65 years.

For doses of 20 mg vortioxetine once daily, the incidences of nausea and constipation were higher in patients aged ≥ 65 years (42% and 15%, respectively) than in patients aged < 65 years (27% and 4%, respectively)(see section 4.4).

Sexual dysfunction

In clinical studies, sexual dysfunction was assessed using the Arizona Sexual Experience Scale (ASEX). Doses of 5 to 15 mg showed no difference to placebo. However, the 20 mg dose of vortioxetine was associated with an increase in sexual dysfunction (TESD) (see section 5.1).

Class effect

Epidemiological studies, mainly conducted in patients 50 years of age and older, show an increased risk of bone fractures in patients receiving a medicinal product from related pharmacological classes of antidepressants (SSRIs or TCAs). The mechanism behind this risk is unknown, and it is not known if this risk is also relevant for vortioxetine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose

Ingestion of vortioxetine in clinical trials in the dose range of 40 mg to 75 mg has caused an aggravation of the following adverse reactions: nausea, postural dizziness, diarrhoea, abdominal discomfort, generalised pruritus, somnolence and flushing.

Post-marketing experience mainly concerns vortioxetine overdoses of up to 80 mg. In the majority of cases, no symptoms or mild symptoms were reported. The most frequently reported symptoms were nausea and vomiting.

There is limited experience with vortioxetine overdoses above 80 mg. Following dosages several fold higher than the therapeutic dose range, events of seizure and serotonin syndrome have been reported.

Management of overdose should consist of treating clinical symptoms and relevant monitoring. Medical follow-up in a specialised environment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychoanaleptics; Other antidepressants, ATC-code: N06AX26

Mechanism of action

The mechanism of action of vortioxetine is thought to be related to its direct modulation of serotonergic receptor activity and inhibition of the serotonin (5-HT) transporter. Nonclinical data indicate that vortioxetine is a 5-HT₃, 5-HT₇, and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist and inhibitor of the 5-HT transporter, leading to modulation of neurotransmission in several systems, including predominantly the serotonin but probably also the norepinephrine, dopamine, histamine, acetylcholine, GABA and glutamate systems. This multimodal activity is considered responsible for the antidepressant and anxiolytic-like effects and the improvement of cognitive function, learning and memory observed with vortioxetine in animal studies. However, the precise contribution of the individual targets to the observed pharmacodynamic profile remains unclear and caution should be applied when extrapolating animal data directly to man.

In humans, two positron emission tomography (PET) studies have been conducted using 5-HT transporter ligands (¹¹C-MADAM or ¹¹C-DASB) to quantify the 5-HT transporter occupancy in the brain across different dose levels. The mean 5-HT transporter occupancy in the *raphe nuclei* was approximately 50% at 5 mg/day, 65% at 10 mg/day and increased to above 80% at 20 mg/day.

Clinical efficacy and safety

The efficacy and safety of vortioxetine have been studied in a clinical programme that included more than 6,700 patients, of whom more than 3,700 were treated with vortioxetine in short-term (≤12 weeks) studies of a major depressive disorder (MDD). Twelve double-blind, placebo controlled, 6/8-week, fixed-dose studies have been conducted to investigate the short-term efficacy of vortioxetine in MDD in adults (including the elderly). The efficacy of vortioxetine was demonstrated with at least one dosage group across 9 of the 12 studies, showing at least a 2-point difference to placebo in the Montgomery and Åsberg Depression Rating Scale (MADRS) or Hamilton Depression Rating Scale 24-item (HAM-D₂₄) total score. This was supported by clinical

relevance as demonstrated by the proportions of responders and remitters and the improvement in the Clinical Global Impression – Global Improvement (CGI-I) score. The efficacy of vortioxetine increased with increasing dose.

The effect in the individual studies was supported by the meta-analysis (MMRM) of the mean change from baseline in MADRS total score at Week 6/8 in the short-term, placebo-controlled studies in adults. In the meta-analysis, the overall mean difference to placebo across the studies was statistically significant: -2.3 points ($p = 0.007$), -3.6 points ($p < 0.001$), and -4.6 points ($p < 0.001$) for the 5, 10, and 20 mg/day doses, respectively; the 15 mg/day dose did not separate from placebo in the meta-analysis, but the mean difference to placebo was -2.6 points. The efficacy of vortioxetine is supported by the pooled responder analysis, in which the proportion of responders ranged from 46% to 49% for vortioxetine versus 34% for placebo ($p < 0.01$; NRI analysis).

Elderly

In the 8-week, double-blind, placebo-controlled, fixed-dose study in elderly depressed patients (aged ≥ 65 years, $n=452$, 156 of whom were on vortioxetine), vortioxetine 5 mg/day was superior to placebo as measured by improvement in the MADRS and HAM-D₂₄ total scores. The effect seen with vortioxetine was a 4.7 point difference to placebo in MADRS total score at Week 8 (MMRM analysis).

Patients with severe depression or with depression and high levels of anxiety symptoms In severely depressed patients (baseline MADRS total score ≥ 30) and in depressed patients with a high level of anxiety symptoms (baseline HAM-A total score ≥ 20) vortioxetine also demonstrated efficacy in the short-term studies in adults (the overall mean difference to placebo in MADRS total score at Week 6/8 ranged from 2.8 to 7.3 points and from 3.6 to 7.3 points, respectively, (MMRM analysis)). In the dedicated study in elderly, vortioxetine was also effective in these patients.

Effects of vortioxetine on the Digit Symbol Substitution Test (DSST), the University of California San Diego Performance-Based Skills Assessment (UPSA) (objective measures) and Perceived Deficits Questionnaire (PDQ) and Cognitive and Physical Functioning Questionnaire CPFQ (subjective measures) scores

The efficacy of vortioxetine (5-20 mg/day) in patients with MDD has been investigated in 2 adult and 1 elderly short-term, placebo-controlled studies.

Vortioxetine had a statistically significant effect versus placebo on the Digit Symbol Substitution Test (DSST), ranging from $\Delta = 1.75$ ($p = 0.019$) to 4.26 ($p < 0.0001$) in the 2 studies in adults and $\Delta = 2.79$ ($p = 0.023$) in the study in the elderly. In the meta-analyses (ANCOVA, LOCF) of the mean change from baseline in DSST number of correct symbols in all 3 studies, vortioxetine separated from placebo ($p < 0.05$) with a standardised effect size of 0.35. When adjusting for the change in MADRS the total score in the meta-analysis of the same studies showed that vortioxetine separated from placebo ($p < 0.05$) with a standardised effect size of 0.24.

One study assessed the effect of vortioxetine on functional capacity using the University of California San Diego Performance-Based Skills Assessment (UPSA). Vortioxetine separated from placebo statistically with results of 8.0 for vortioxetine versus 5.1 points for placebo ($p=0.0003$).

In one study, vortioxetine was superior to placebo on subjective measures, evaluated using the Perceived Deficits Questionnaire with results of -14.6 for vortioxetine and -10.5 for placebo ($p=0.002$). Vortioxetine did not separate from placebo on subjective

measures when evaluated using the Cognitive and Physical Functioning Questionnaire with results of -8.1 for vortioxetine versus -6.9 for placebo ($p=0.086$).

Tolerability and safety

The safety and tolerability of vortioxetine have been established in short-term studies (6- 8 weeks) across the dose range of 5 to 20 mg/day. For information on undesirable effects, see section 4.8.

Vortioxetine did not increase the incidence of insomnia or somnolence relative to placebo.

The incidence of self-reported adverse sexual reactions was low and similar to placebo in clinical short-term studies with vortioxetine. In studies using the Arizona Sexual Experience Scale (ASEX), the incidence of treatment-emergent sexual dysfunction (TESD) and the ASEX total score showed no clinically relevant difference to placebo in symptoms of sexual dysfunction at the 5 to 15 mg/day doses of vortioxetine. For the 20 mg/day dose, an increase in TESD was seen compared to placebo (an incidence difference of 14.2%, 95% CI [1.4, 27.0]).

The effect of vortioxetine on sexual function was further evaluated in an 8-week, double-blind, flexible-dose, comparative study ($n=424$) versus escitalopram in patients treated for at least 6 weeks with an SSRI (citalopram, paroxetine, or sertraline), with a low level of depressive symptoms (baseline CGI-S ≤ 3) and TESD induced by the prior SSRI treatment. Vortioxetine 10-20 mg/day had statistically significantly less TESD than escitalopram 10-20 mg/day as measured by change in the CSFQ-14 total score (2.2 points, $p=0.013$) at week 8. The proportion of responders was not significantly different in the vortioxetine group (162 (74.7%)) compared with the escitalopram group (137 (66.2%)) at week 8 (OR 1.5 $p=0.057$). The antidepressant effect was maintained in both treatment groups.

Vortioxetine had no effect relative to placebo on body weight, heart rate, or blood pressure in clinical short-term studies.

No clinically significant changes were observed in hepatic or renal assessments in clinical studies.

Vortioxetine has not shown any clinically significant effect on ECG parameters, including the QT, QTc, PR and QRS intervals, in patients with MDD. In a thorough QTc study in healthy subjects at doses up to 40 mg daily, no potential for the prolongation of the QTc interval was observed.

Paediatric population

Clinical studies on the use of Brintellix in children and adolescents have not been conducted; therefore, the safety and efficacy of Brintellix in the paediatric population have not been established (see section 4.2).

5.2 Pharmacokinetic properties

Absorption

Vortioxetine is slowly, but well absorbed after oral administration and the peak plasma concentration is reached within 7 to 11 hours. Following multiple dosing of 5, 10, or 20 mg/day, mean $C_{\max}$ values of 9 to 33 ng/mL were observed. The absolute bioavailability is 75%. No effect of food on the pharmacokinetics was observed (see section 4.2).

Distribution

The mean volume of distribution (V_{ss}) is 2,600 L, indicating extensive extravascular distribution. Vortioxetine is highly bound to plasma proteins (98 to 99%) and the binding appears to be independent of vortioxetine plasma concentrations.

Biotransformation

Vortioxetine is extensively metabolised in the liver, primarily through oxidation catalysed by CYP2D6 and to a minor extent CYP3A4/5 and CYP2C9, and subsequent glucuronic acid conjugation.

No inhibitory or inducing effect of vortioxetine was observed in the drug-drug interaction studies for the CYP isozymes CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A4/5 (see section 4.5). Vortioxetine is a poor P-gp substrate and inhibitor.

The major metabolite of vortioxetine is pharmacologically inactive.

Elimination

The mean elimination half-life and oral clearance are 66 hours and 33 L/h, respectively. Approximately 2/3 of the inactive vortioxetine metabolites are excreted in the urine and approximately 1/3 in the faeces. Only negligible amounts of vortioxetine are excreted in the faeces. Steady-state plasma concentrations are achieved in approximately 2 weeks.

Linearity/non-linearity

The pharmacokinetics are linear and time independent in the dose range studied (2.5 to 60 mg/day).

In accordance with the half-life, the accumulation index is 5 to 6 based on AUC_{0-24h} following multiple doses of 5 to 20 mg/day.

Special populations

Elderly

In elderly healthy subjects (aged ≥ 65 years; $n=20$), the exposure to vortioxetine increased up to 27% ($C_{\max}$ and AUC) compared to young healthy control subjects (aged ≤ 45 years)

after multiple doses of 10 mg/day. The lowest effective dose of 5 mg vortioxetine once daily should always be used as the starting dose in patients ≥ 65 years (see section 4.2). However, caution should be exercised when prescribing to elderly patients at doses higher than 10 mg vortioxetine once daily (see section 4.4).

CYP2D6 gene types

The plasma concentration of vortioxetine was approximately two times higher in CYP2D6 poor metabolisers than in extensive metabolisers. Co-administration of strong CYP3A4/2C9 inhibitors to CYP2D6 poor metabolisers could potentially result in higher exposure (see section 4.5).

In CYP2D6 ultra-rapid metabolisers, the plasma concentration of vortioxetine 10 mg/day were between those obtained in extensive metabolisers at 5 mg/day and 10 mg/day. Depending on individual patient response, a dose adjustment may be considered (see section 4.2).

5.3 Preclinical safety data

Administration of vortioxetine in the general toxicity studies in mice, rats and dogs was mainly associated with CNS-related clinical signs. These included salivation (rat and dog), pupil dilatation (dog), and two incidences of convulsions in dogs in the general toxicity study programme. A no-effect level for convulsions was established with a corresponding safety margin of 5 considering the maximum recommended therapeutic dose of 20 mg/day. Target organ toxicity was restricted to kidneys (rats) and liver (mice and rats). The changes in the kidney in rats (glomerulonephritis, renal tubular obstruction, crystalline material in renal tubule) and in the liver of mice and rats (hepatocellular hypertrophy, hepatocyte necrosis, bile duct hyperplasia, crystalline material in bile ducts) were seen at exposures more than 10-fold (mice) and 2-fold (rats) the human exposure at the maximum recommended therapeutic dose of 20 mg/day. These findings were mainly attributed to rodent-specific vortioxetine-related crystalline material obstruction of the renal tubules and the bile ducts, respectively, and considered of low risk to humans.

Vortioxetine was not genotoxic in a standard battery of in vitro and in vivo tests.

Based on results from conventional 2-year carcinogenicity studies in mice or rats, vortioxetine is not considered to pose a risk of carcinogenicity in humans.

Vortioxetine had no effect on rat fertility, mating performance, reproductive organs, or sperm morphology and motility. Vortioxetine was not teratogenic in rats or rabbits, but reproductive toxicity in terms of effects on foetal weight and delayed ossification were seen in the rat at exposures more than 10-fold the human exposure at the maximum recommended therapeutic dose of 20 mg/day. Similar effects were seen in the rabbit at sub-therapeutic exposure.

In a pre- and post-natal study in rats, vortioxetine was associated with increased pup mortality, reduced bodyweight gain, and delayed pup development at doses that did not

result in maternal toxicity and with associated exposures similar to those achieved in humans following administration of vortioxetine 20 mg/day (see section 4.6).

Vortioxetine-related material was distributed to the milk of lactating rats (see section 4.6).

In juvenile toxicity studies in rats, all vortioxetine treatment-related findings were consistent with those noted in adult animals.

Environmental risk assessment studies have shown that vortioxetine has the potential to be persistent, bioaccumulative and toxic to the environment (risk to fish). However, by recommended patient usage vortioxetine is considered to pose negligible risk to the aquatic and terrestrial environment (see section 6.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core of Brintellix 5 mg, 10 mg, & 20 mg film-coated tablets

Mannitol
Microcrystalline cellulose
Hydroxypropylcellulose
Sodium starch glycolate (type A)
Magnesium stearate

Tablet coating of Brintellix 5 mg film-coated tablets

Hypromellose
Macrogol 400
Titanium dioxide
(E171) Iron oxide
red (E172)

Tablet coating of Brintellix 10 mg film-coated tablets

Hypromellose
Macrogol 400
Titanium dioxide
(E171) Iron oxide
yellow (E172)

Tablet coating of Brintellix 20 mg film-coated tablets

Hypromellose
Macrogol 400
Titanium dioxide
(E171) Iron oxide
red (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Blister: Transparent; PVC/PVdC/aluminium

blister. Pack sizes:

5 mg: 28 film-coated tablets.

10 mg: 28 film-coated tablets.

20 mg: 28 film-coated tablets.

6.6 Special precautions for disposal

This medicinal product may pose a risk to the environment (see section 5.3).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER

H. Lundbeck A/S

Ottiliavej 9

2500 Valby

Denmark

HARUS DENGAN RESEP DOKTER

Registration No.

Brintellix 5 mg: DKI1799900717A1

Brintellix 10 mg: DKI1799900717B1

Brintellix 20 mg: DKI1799900717C1

Registered by:

PT. Pyridam Farma Tbk,

Jakarta, Indonesia

Brintellix® film-coated tablets
vortioxetine

Informasi Produk untuk Pasien

Baca isi leaflet ini dengan seksama sebelum Anda mulai menggunakan obat ini karena leaflet ini mengandung informasi yang penting bagi Anda.

- Simpan leaflet ini. Anda mungkin perlu membaca lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker.
- Obat ini diresepkan hanya untuk Anda. Jangan menyebarkannya kepada orang lain. Ini dapat membahayakan mereka, bahkan jika ada tanda-tanda mereka memiliki penyakit yang sama dengan Anda.
- Jika Anda mengalami efek samping, hubungi dokter atau apoteker. Ini termasuk efek samping yang mungkin tidak tercantum dalam leaflet ini. Lihat bagian 4.

Apa informasi yang ada pada leaflet ini

1. Apakah Brintellix dan apa kegunaannya
2. Hal yang perlu diketahui sebelum menggunakan Brintellix
3. Bagaimana cara mengonsumsi Brintellix
4. Efek samping yang mungkin terjadi
5. Bagaimana cara menyimpan Brintellix
6. Isi kemasan dan informasi lain

1. Apakah Brintellix dan apa kegunaannya

Brintellix mengandung zat aktif vortioxetine, yang termasuk dalam kelompok obat yang disebut antidepresan.

Brintellix digunakan untuk mengobati *major depressive disorder* pada orang dewasa.

Brintellix telah terbukti mengurangi berbagai gejala depresi, termasuk kesedihan, ketegangan batin (perasaan cemas), gangguan tidur (tidur berkurang), nafsu makan berkurang, sulit berkonsentrasi, perasaan tidak berharga, kehilangan minat dalam kegiatan favorit, perasaan terasa melambat.

2. Hal yang perlu diketahui sebelum menggunakan Brintellix

Jangan menggunakan Brintellix:

- Jika Anda alergi terhadap vortioxetine atau salah satu bahan lain dari obat ini (tercantum dalam bagian 6).
- Jika Anda menggunakan obat lain untuk depresi dari golongan obat non-selektif monoamine oxidase inhibitors atau inhibitor MAO-A. Tanyakan kepada dokter Anda jika Anda tidak yakin.

Peringatan dan Perhatian

Bicaralah dengan dokter atau apoteker sebelum menggunakan Brintellix jika Anda :

- Sedang menggunakan obat lain yang dikenal dengan efek serotonergik, seperti:
- Tramadol (obat penghilang rasa sakit yang kuat).

- Sumatriptan dan obat sejenis dengan nama zat aktif berakhiran "triptans" (digunakan untuk mengobati migrain).
Menggunakan obat ini bersama-sama dengan Brintellix dapat menyebabkan sindrom serotonin. Sindrom ini mungkin berhubungan dengan halusinasi, berkedut tak sadar, mempercepat detak jantung, tekanan darah tinggi, demam, mual dan diare
- Pernah kejang
Dokter Anda akan merawat Anda dengan hati-hati jika Anda memiliki riwayat kejang atau gangguan kejang yang tidak stabil / epilepsi. Kejang memiliki risiko potensial dengan obat-obatan yang digunakan untuk mengobati depresi. Pengobatan harus dihentikan pada pasien yang memiliki kemungkinan kejang atau di mana ada peningkatan frekuensi kejang.
- Mengidap mania
- Memiliki kecenderungan untuk pendarahan atau memar dengan mudah.
- Memiliki kadar natrium yang rendah dalam darah.
- Berumur diatas 65 tahun.
- Obat ini tidak digunakan untuk pasien dengan gangguan fungsi ginjal dan hati.
- Memiliki atau sebelumnya pernah mengalami peningkatan tekanan pada mata atau glaucoma. Jika mata Anda menjadi nyeri dan Anda mengalami penglihatan kabur selama pengobatan, hubungi dokter Anda.

Saat Anda menjalani pengobatan antidepresan, termasuk vortioxetine, Anda mungkin juga mengalami perasaan agresi, agitasi, amarah dan mudah tersinggung. Jika ini terjadi, Anda harus berbicara dengan dokter Anda.

Pikiran bunuh diri dan memburuknya depresi Anda

Jika Anda mengalami depresi dan / atau memiliki gangguan kecemasan, kadangkala anda dapat memiliki pikiran untuk menyakiti atau membunuh dirimu sendiri. Hal ini dapat meningkat ketika pertama kali memulai antidepresan, karena obat-obat ini semua membutuhkan waktu untuk bekerja, biasanya sekitar dua minggu tapi terkadang lebih lama.

Anda mungkin akan cenderung untuk berpikir seperti ini jika Anda:

- Sebelumnya telah memiliki pengalaman tentang membunuh atau melukai diri sendiri.
- Adalah dewasa muda.

Informasi dari uji klinis telah menunjukkan peningkatan risiko perilaku bunuh diri pada orang dewasa berusia kurang dari 25 tahun dengan kondisi kejiwaan yang dirawat dengan antidepresan.

Jika sesaat anda memiliki pikiran untuk menyakiti atau membunuh diri sendiri, segera hubungi dokter atau langsung pergi ke rumah sakit. Anda mungkin merasa perlu untuk memberitahu teman atau kerabat dekat bahwa anda mengalami depresi atau memiliki gangguan kecemasan, dan mintalah mereka untuk membaca leaflet ini. Mintalah mereka untuk memberitahu Anda jika mereka berpikir depresi atau kecemasan anda menjadi semakin parah, atau jika mereka khawatir tentang perubahan perilaku Anda.

Anak- anak dan Remaja

Brintellix tidak dianjurkan untuk digunakan pada anak-anak dan remaja di bawah 18 tahun karena kurangnya informasi untuk kelompok usia ini.

Pengobatan lainnya dan Brintellix

Beritahu dokter atau apoteker Anda jika Anda menggunakan, baru-baru ini menggunakan atau mungkin menggunakan obat-obatan lain.

Tolong beritahu dokter Anda jika Anda sedang mengonsumsi obat-obatan berikut:

- phenelzine, iproniazid, isocarboxazid, nialamide, tranylcypromine (obat-obatan untuk mengobati depresi yang dikenal sebagai *non-selective monoamine oxidase inhibitors*); Anda tidak boleh menggunakan obat-obatan ini bersama dengan Brintellix. Jika Anda telah menggunakan salah satu dari obat-obatan ini, Anda harus menunggu 14 hari sebelum Anda mulai menggunakan Brintellix. Setelah berhenti menggunakan Brintellix, Anda harus menunggu 14 hari sebelum menggunakan obat-obatan ini.
- Moclobemide (obat untuk mengobati depresi).
- Selegiline, rasagiline (obat-obatan untuk mengobati penyakit Parkinson).
- Linezolid (obat untuk mengobati infeksi bakteri).
- Lithium (obat untuk mengobati depresi dan gangguan mental) atau triptofan.
- Obat diketahui menyebabkan tingkat natrium yang rendah.
- Rifampisin (obat untuk mengobati tuberkulosis dan infeksi lainnya).
- Carbamazepine, phenytoin (obat-obatan untuk mengobati epilepsi atau penyakit lainnya).
- Warfarin, dipyridamole, phenprocoumon, dosis rendah asam asetilsalisilat (obat pengencer darah).

Obat-obatan yang meningkatkan risiko kejang:

- Sumatriptan dan obat-obatan yang sama dengan nama zat aktif berakhiran "triptans".
- Tramadol (obat penghilang rasa sakit yang kuat).
- Mefloquin (obat untuk mencegah dan mengobati malaria).
- Bupropion (obat untuk mengobati depresi juga digunakan untuk menyapih dari merokok).
- Fluoxetine, paroxetine dan obat-obatan lain untuk mengobati depresi yang disebut SSRI / SNRIs, trisiklik.
- St John Wort (*hypericum perforatum*) (obat untuk mengobati depresi).
- Quinidine (obat untuk mengobati gangguan irama jantung).
- Klorpromazin, chlorprothixene, haloperidol (obat-obatan untuk mengobati gangguan mental milik kelompok yang disebut fenotiazin, thioxanthenes, butyrophenones).

Tolong beritahu dokter Anda jika Anda sedang mengonsumsi obat-obatan di atas, karena dokter Anda perlu tahu jika Anda sudah berada pada risiko kejang.

Jika Anda menjalani skrining obat urin, mengonsumsi Brintellix dapat menyebabkan hasil positif untuk metadon saat beberapa metode tes digunakan, meskipun Anda

mungkin tidak menggunakan metadon. Jika ini terjadi, tes yang lebih khusus dapat dilakukan.

Brintellix dan alkohol

Tidak dianjurkan menggabungkan obat ini dengan alkohol

Kehamilan, menyusui dan kesuburan

Bila Anda sedang hamil atau menyusui, berfikir mungkin Anda hamil atau sedang merencanakan kehamilan, konsultasikan kepada dokter Anda sebelum Anda mengkonsumsi obat ini.

Kehamilan

Brintellix sebaiknya tidak digunakan selama kehamilan kecuali dokter mengatakan mutlak diperlukan.

Bila Anda mengkonsumsi obat untuk mengobati depresi, termasuk Brintellix, selama 3 bulan terakhir kehamilan Anda, Anda harus menyadari efek berikut mungkin akan tampak pada bayi Anda ketika baru lahir: masalah dengan pernapasan, kulit kebiruan, kejang, perubahan suhu tubuh, kesulitan makan, muntah, gula darah rendah, otot kaku atau terkulai, refleks yang nyata, tremor, gelisah, lekas marah, lesu, terus-menerus menangis, mengantuk dan kesulitan tidur. Segera hubungi dokter jika bayi Anda yang baru lahir memiliki gejala-gejala tersebut.

Pastikan bidan dan/atau dokter Anda tahu bahwa Anda mengkonsumsi Brintellix. Ketika digunakan selama kehamilan, terutama dalam 3 bulan terakhir kehamilan, obat-obatan seperti Brintellix dapat meningkatkan risiko kondisi serius pada bayi, seperti persistent pulmonary hypertension of the newborn (PPHN), membuat bayi bernapas lebih cepat dan nampak kebiru-biruan. Gejala ini biasanya dimulai selama 24 jam pertama setelah bayi lahir. Jika ini terjadi pada bayi Anda, segera hubungi bidan dan / atau dokter.

Menyusui

Kandungan Brintellix diperkirakan akan masuk ke dalam ASI. Brintellix tidak untuk digunakan selama menyusui. Dokter Anda akan membuat keputusan apakah Anda harus berhenti menyusui, atau berhenti menggunakan Brintellix dengan memperhitungkan manfaat menyusui bagi anak Anda, dan manfaat terapi untuk Anda.

Mengemudi dan menggunakan mesin

Brintellix tidak memiliki pengaruh pada kemampuan untuk mengemudi dan menggunakan mesin. Namun, karena efek samping seperti pusing telah dilaporkan, disarankan tetap berhati-hati selama melakukan kegiatan tersebut saat memulai pengobatan Brintellix atau mengubah dosis.

Brintellix mengandung Natrium

Obat ini mengandung kurang dari 1 mmol natrium (23 mg) per tablet, artinya 'bebas natrium'.

3. Bagaimana cara mengonsumsi Brintellix

Selalu minum obat ini persis seperti yang dokter Anda katakan kepada Anda. Periksa ke dokter atau apoteker Anda jika Anda tidak yakin.

Dosis Brintellix yang dianjurkan adalah 10 mg vortioxetine diminum sekali sehari. Dosis dapat ditingkatkan oleh dokter Anda sampai maksimal 20 mg vortioxetine per hari atau diturunkan sampai minimum 5 mg vortioxetine per hari tergantung pada respons Anda terhadap pengobatan. Untuk pasien berumur 65 tahun atau lebih, dosis awal adalah 5 mg sekali sehari.

Cara Pemberian

Minum satu tablet dengan segelas air.

Tablet dapat diminum dengan atau tanpa makanan.

Lama Pengobatan

Minum Brintellix selama yang dianjurkan oleh dokter Anda.

Jika Anda meminum Brintellix lebih dari yang seharusnya

Jika Anda meminum Brintellix lebih dari dosis yang ditentukan, segera hubungi dokter atau gawat darurat rumah sakit terdekat. Simpan wadah dan tablet yang tersisa jika ada. Lakukan ini bahkan jika tidak ada tanda-tanda ketidaknyamanan. Tanda-tanda overdosis adalah pusing, mual, diare, perut tidak nyaman, gatal-gatal pada seluruh tubuh, mengantuk dan kemerahan.

Setelah asupan dosis beberapa kali lebih tinggi dari dosis yang ditentukan tersebut, kejang dan kondisi yang jarang terjadi yang dikenal sebagai serotonin syndrome telah dilaporkan.

Jika Anda lupa meminum Brintellix

Minum dosis selanjutnya seperti waktu biasanya. Jangan meminum dosis ganda untuk menggantikan dosis yang terlupakan.

Jika anda berhenti minum Brintellix

Jangan berhenti minum Brintellix tanpa berbicara dengan dokter anda.

Jika anda memiliki pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan kepada dokter atau apoteker

4. Efek samping yang mungkin terjadi

Seperti semua obat, obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Secara umum, efek samping yang teramati adalah ringan sampai sedang dan terjadi dalam dua minggu pertama pengobatan. Reaksi yang biasanya bersifat sementara dan tidak menyebabkan penghentian terapi.

Efek samping yang tercantum di bawah ini telah dilaporkan dalam frekuensi berikut.

Sangat umum: dapat mempengaruhi lebih dari 1 dalam 10 orang

- mual

Umum: dapat mempengaruhi hingga 1 dari 10 orang

- Diare, sembelit, muntah
- pusing
- Gatal seluruh tubuh
- Mimpi abnormal

Jarang: dapat mempengaruhi hingga 1 dari 100 orang

- flushing
- Berkeringat di malam hari

Sangat jarang: dapat mempengaruhi hingga 1 dari 1.000 orang

- pupil membesar (mydriasis), yang dapat meningkatkan risiko glaukoma (lihat bagian 2)

Frekuensi tidak diketahui:

- kadar natrium yang rendah dalam darah (gejala dapat termasuk perasaan pusing, lemah, bingung, mengantuk atau sangat lelah, atau perasaan atau benar sakit; gejala yang lebih serius adalah pingsan, kejang, atau jatuh).
- serotonin syndrome (lihat bagian 2).
- reaksi alergi, yang mungkin serius, menyebabkan pembengkakan wajah, bibir, lidah atau tenggorokan, kesulitan bernapas atau menelan, dan / atau penurunan tekanan darah secara tiba-tiba (membuat Anda merasa pusing atau lengah)
- gatal-gatal
- perdarahan yang berlebihan atau tidak dapat dijelaskan (termasuk memar, pendarahan hidung, gastrointestinal dan pendarahan vagina)
- ruam
- gangguan tidur (insomnia)
- agitasi dan agresi. Jika Anda mengalami efek samping ini, hubungi dokter Anda (lihat bagian 2).

Peningkatan risiko patah tulang terlihat pada pasien yang memakai obat-obat sejenis.

Pelaporan efek samping

Jika Anda merasakan efek samping apapun, konsultasikan dengan dokter Anda atau apoteker. Efek yang dirasakan termasuk efek-efek yang tidak terdaftar dalam brosur ini. Anda juga dapat melaporkan efek samping secara langsung melalui sistem pelaporan nasional. Dengan melaporkan efek samping tersebut, Anda dapat membantu menyediakan lebih banyak informasi keamanan dari obat ini.

5. Bagaimana cara menyimpan Brintellix

Jangan disimpan diatas 30°C

Jauhkan obat ini dari jangkauan anak-anak.

Jangan gunakan obat setelah tanggal kadaluarsa yang tercantum pada kemasan. Tanggal kadaluarsa mengacu pada hari terakhir dari bulan itu.

Jangan membuang obat melalui air limbah. Konsultasikan kepada apoteker Anda, bagaimana membuang obat yang tidak Anda gunakan lagi. Hal ini akan membantu melindungi lingkungan.

Batas Waktu Penyimpanan

48 Bulan

6. Isi kemasan dan informasi lain

5 mg vortioxetine, tablet salut selaput

Apa kandungan Brintellix

- Zat aktif adalah vortioxetine. Tiap tablet salut selaput mengandung 5 mg vortioxetine (sebagai hidrobromida).
- Komposisi lainnya adalah manitol (E421), selulosa mikrokrystalin, hidroksipropilselulosa, glikolat pati sodium (tipe A), magnesium stearat, hipromelosa, Macrogol 400, titanium dioksida (E171), besi oksida merah (E172).

Bagaimana tampilan Brintellix dan isi kemasan

Pink, tablet salut selaput (tablet) berbentuk seperti almond 5 x 8,4 mm ditandai “TL” di satu sisi dan “5” di sisi lain.

Tablet salut selaput Brintellix 5 mg tersedia dalam kemasan blister 28 tablet.

10 mg vortioxetine, tablet salut selaput

Apa kandungan Brintellix

- Zat aktif adalah vortioxetine. Tiap tablet salut selaput mengandung 10 mg vortioxetine (sebagai hidrobromida).
- Komposisi lainnya adalah manitol (E421), selulosa mikrokrystalin, hidroksipropilselulosa, glikolat pati sodium (tipe A), magnesium stearat, hipromelosa, Macrogol 400, titanium dioksida (E171), besi oksida kuning (E172).

Bagaimana tampilan Brintellix dan isi kemasan

Kuning, tablet salut selaput (tablet) berbentuk seperti almond 5 x 8,4 mm ditandai “TL” di satu sisi dan “10” di sisi lain.

Tablet salut selaput Brintellix 10 mg tersedia dalam kemasan blister 28 tablet.

20 mg vortioxetine, tablet salut selaput

Apa kandungan Brintellix

- Zat aktif adalah vortioxetine. Tiap tablet salut selaput mengandung 20 mg vortioxetine (sebagai hidrobromida).
- Komposisi lainnya adalah manitol (E421), selulosa mikrokrystalin, hidroksipropilselulosa, glikolat pati sodium (tipe A), magnesium stearat, hipromelosa, Macrogol 400, titanium dioksida (E171), besi oksida merah (E172).

Bagaimana tampilan Brintellix dan isi kemasan

Merah, tablet salut selaput (tablet) berbentuk seperti almond 5 x 8,4 mm ditandai “TL” di satu sisi dan “20” di sisi lain.

Tablet salut selaput Brintellix 20 mg tersedia dalam kemasan blister 28 tablet.

Diproduksi oleh:

H. Lundbeck A/S
Ottiliavej 9
2500 Valby
Denmark

HARUS DENGAN RESEP DOKTER

Nomor Registrasi:

Brintellix 5 mg : DKI1799900717A1

Brintellix 10 mg : DKI1799900717B1

Brintellix 20 mg : DKI1799900717C1

Diregistrasikan oleh:

PT. Pyridam Farma

Jakarta – Indonesia

Leaflet ini direvisi pada bulan Oktober 2020