PACKAGE LEAFLET

Package leaflet: Information for the patient

Zismirt orotab 15 mg orodispersible tablets
Zismirt orotab 30 mg orodispersible tablets
Zismirt orotab 45 mg orodispersible tablets
mirtazapine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Zismirt orotab is and what it is used for

Zismirt orotab is one of a group of medicines called **antidepressants**.
Zismirt orotab is used to treat depressive illness in adults.

2. What you need to know before you take Zismirt orotab

Do not take Zismirt orotab:
- if you are allergic to mirtazapine or any of the other ingredients of this medicine (listed in section 6).
- if you are taking or have recently taken (within the last two weeks) medicines called monoamine oxidase inhibitors (MAO inhibitors).

Warnings and precautions

Do not take or tell your doctor before taking Zismirt orotab:
If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Zismirt orotab or other medicines. Serious skin reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with the use of Zismirt orotab. Stop using and seek medical attention immediately if you notice any of the symptoms described in section 4 in relation to these serious skin reactions. If you have ever developed any severe skin reactions, treatment with Zismirt orotab should not be restarted

Children and adolescents
Zismirt orotab should normally not be used for children and adolescents under 18 years because efficacy was not demonstrated. Also, you should know that patients under 18 have an increased risk of side effects such as suicide attempt, suicidal thoughts and hostility (predominately aggression, oppositional behaviour and anger) when they take this class of medicine. Despite this, your doctor may

prescribe Zismirt orotab for patients under 18 because he/she decides that this is in their best interests. If the doctor has prescribed Zismirt orotab for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking Zismirt orotab. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Zismirt orotab in this age group have not yet been demonstrated. In addition, significant weight gain has been observed in this age category more often when treated with Zismirt orotab compared with adults.

Thoughts of suicide and worsening of your depression
If you are depressed you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer.
You may be more likely to think like this:

- if you have previously had thoughts about killing or harming yourself.
- if you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in 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.

You may find it helpful to tell a relative or close friend that you are depressed, and ask them to read this leaflet. You might ask them to tell you if they think your depression is getting worse, or if they are worried about changes in your behaviour.

Talk to your doctor or pharmacist before taking Zismirt orotab if you have, or have ever had one of the following conditions.

- **seizures** (epilepsy).
- **liver disease**, including jaundice.
- **kidney disease**.
- **heart disease or a family history of heart disease**, including certain kinds of heart conditions that may change your heart rhythm, a recent heart attack, heart failure, or if you are taking certain medicines that may affect the heart's rhythm.
- **low blood pressure**.
- **schizophrenia**.
- **bipolar disorder** (alternating periods of feeling elated/overactivity and depressed mood).
- **diabetes** (you may need to adjust your dose of insulin or other antidiabetic medicines).
- **eye disease**, such as increased pressure in the eye (glaucoma).
- **difficulty in passing water** (urinating), which might be caused by an enlarged prostate.

Elderly patients

- if you are an elderly person. You could be more sensitive to the side-effects of antidepressants.

During treatment
Talk to your doctor:

- if you develop signs of infection such as high fever, sore throat and mouth ulcers.
  In rare cases these symptoms can be a sign of disturbances in blood cell production in the bone marrow. While rare, these symptoms most commonly appear after 4-6 weeks of treatment.

Other medicines and Zismirt orotab

Do not take Zismirt orotab in combination with:

- **monoamine oxidase inhibitors** (MAO inhibitors). Also, do not take Zismirt orotab during the two weeks after you have stopped taking MAO inhibitors. If you stop taking Zismirt orotab, do not take MAO inhibitors during the next two weeks either.

Examples of MAO inhibitors are moclobemide, tranylcypromine (both are antidepressants) and selegiline (used for Parkinson's disease).

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription, especially any of the following:

- **antidepressants such as SSRIs** (e.g. citalopram)**, venlafaxine and L-tryptophan, or triptans** (used to treat migraine e.g. sumatriptan), **tramadol** (a pain-killer), **linezolid** (an antibiotic), **lithium** (used to treat some psychiatric conditions), **methylene blue** (used to treat some types of blood poisoning **and St. John's Wort – *Hypericum perforatum* preparations** (a herbal remedy for depression). In very rare cases Zismirt orotab alone or the combination of Zismirt orotab with these medicines, can lead to a so-called serotonin syndrome. Some of the signs of this syndrome are: fever, sweating, increased heart rate, diarrhoea, (uncontrollable) muscle contractions, shivering, overactive reflexes, restlessness, mood changes, and unconsciousness. If you get a combination of these signs, talk to your doctor immediately;
- **medicines for anxiety or insomnia** such as benzodiazepines e.g. diazepam, chlordiazepoxide;
- **medicines for schizophrenia** such as olanzapine;
- **medicines for allergies** such as cetirizine;
- **medicines for severe pain** such as morphine. In combination with these medicines mirtazapine can increase the drowsiness caused by these medicines.

These medicines increase the amount of mirtazapine in your blood:

- **medicines for infections**; medicines for bacterial infections (such as erythromycin); medicines for fungal infections (such as ketoconazole), medicines for HIV/AIDS (such as HIV- protease inhibitors e.g. ritonavir, nelfinavir); **medicines for depression** (such as nefazodone) and **medicines for stomach ulcers** (such as cimetidine). In combination with Zismirt orotab these medicines can increase the amount of mirtazapine in your blood. Inform your doctor if you are using these medicines. It might be needed to lower the dose of Zismirt orotab, or when these medicines are stopped, to increase the dose of Zismirt orotab again.

These medicines decrease the amount of mirtazapine in your blood:

- **carbamazepine and phenytoin,** medicines for epilepsy; **rifampicin,** medicines for tuberculosis. In combination with Zismirt orotab these medicines can reduce the amount of mirtazapine in your blood. Inform your doctor if you are using these medicines. It might be needed to increase the dose of Zismirt orotab, or when these medicines are stopped to lower the dose of Zismirt orotab again.
- **warfarin,** a medicine to prevent blood clotting. Zismirt orotab can increase the effects of warfarin on the blood. Inform your doctor if you are using this medicine. In case of combination it is advised that a doctor monitors your blood carefully.

Zismirt orotab with alcohol
You may get drowsy if you drink alcohol while you are taking Zismirt orotab.
You are advised not to drink any alcohol.

Pregnancy and breast-feeding
Limited experience with mirtazapine administration to pregnant women does not indicate an increased risk. However, caution should be exercised when used during pregnancy.

If you are taking Zismirt orotab and you become pregnant or you plan to get pregnant, ask your doctor whether you may continue taking Zismirt orotab. If you use Zismirt orotab until, or shortly before birth, your baby should be supervised for possible adverse effects.

Make sure your midwife and/or doctor knows you are on Zismirt orotab.

When taken during pregnancy, similar drugs (SSRIs) 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.

Ask your doctor whether you can breast-feed, while taking Zismirt orotab.

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.

Driving and using machines
Zismirt orotab can affect your concentration or alertness. Make sure these abilities are not affected before you drive or operate machinery.

Zismirt orotab contains aspartame
This medicine contains 3 mg, 6 mg or 9 mg aspartame in each 15 mg, 30 mg or 45 mg orodispersible tablet, respectively. Aspartame is a source of phenylalanine. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

3. How to take Zismirt orotab

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take
The recommended dose is 15 or 30 mg every day. Your doctor may advise you to increase your dose after a few days to the amount that is best for you (between 15 and 45 mg per day). The recommended dose is usually the same for all ages. However, if you are an elderly person or if you have kidney or liver disease, your doctor may change the dose.

When to take Zismirt orotab
Take Zismirt orotab at the same time each day.
It is best to take Zismirt orotab as a single dose before you go to bed. However your doctor may suggest to split your dose of Zismirt orotab – once in the morning and once at night-time before you go to bed. The higher dose should be taken before you go to bed.

Take the orodispersible tablet as follows
Take your tablets orally.

1. **Do not crush the orodispersible tablet**
   In order to prevent crushing the orodispersible tablet, do not push against the tablet pocket (Figure A).

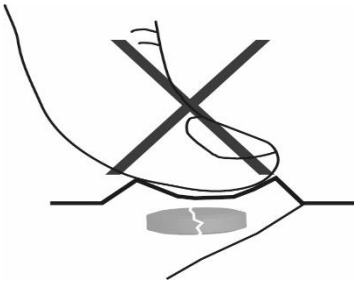

   Fig. A.

2. **Tear off one tablet pocket**

Each blister contains tablet pockets, which are separated by perforations. Tear off one tablet pocket along the dotted lines (Figure 1).

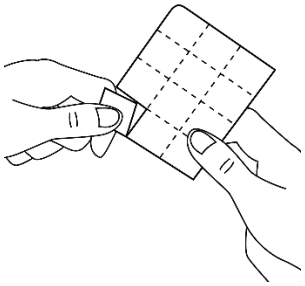

Fig. 1.

3. **Peel off the lid**
   Carefully peel off the lidding foil, starting in the corner (Figure 2).

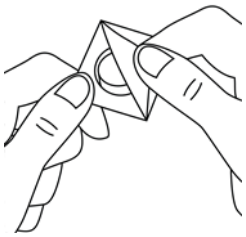

Fig. 2.

4. **Take out the orodispersible tablet**
   Take out the orodispersible tablet with dry hands and place it on the tongue.
   (Figure 3).

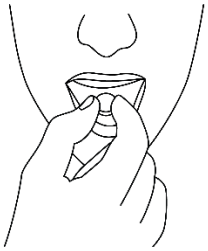

Fig. 3.
It will rapidly disintegrate and can be swallowed without water.

When can you expect to start feeling better
Usually Zismirt orotab will start working after 1 to 2 weeks and after 2 to 4 weeks you may start to feel better. It is important that, during the first few weeks of the treatment, you talk with your doctor about the effects of Zismirt orotab:
2 to 4 weeks after you have started taking Zismirt orotab, talk to your doctor about how this medicine has affected you.
If you still don't feel better, your doctor may prescribe a higher dose. In that case, talk to your doctor again after another 2 to 4 weeks. Usually you will need to take Zismirt orotab until your symptoms of depression have disappeared for 4 to 6 months.

Use in children and adolescents under the age of 18 years:
Zismirt orotab should not be used in children and adolescents under the age of 18 years. (see section 2 'Children and adolescents under 18 years of age').

If you take more Zismirt orotab than you should
If you or someone else have taken too much Zismirt orotab, call a doctor straight away.
The most likely signs of an overdose of Zismirt orotab (without other medicines or alcohol) are drowsiness, disorientation, changes to your heart rhythm (fast, irregular heartbeat) and/or fainting which could be symptoms of a life-threatening condition known as torsade de pointes.

If you forget to take Zismirt orotab
If you are supposed to take your dose **once a day**
If you have forgotten to take your dose of Zismirt orotab, do not take the missed dose. Just skip it. Take your next dose at the normal time.

Do not take a double dose to make up for a forgotten tablet.

If you are supposed to take your dose **twice a day**
If you have forgotten to take your morning dose, simply take it together with your evening dose.
If you have forgotten to take your evening dose, do not take it with the next morning dose; just skip it and continue with your normal morning and evening doses.
If you have forgotten to take both doses, do not attempt to make up for the missed doses. Skip both doses and continue the next day with your normal morning and evening doses.

If you stop taking Zismirt orotab
Only stop taking Zismirt orotab after speaking to your doctor.
If you stop too early, your depression might come back. Once you are feeling better, talk to your doctor. Your doctor will decide when treatment can be stopped.
Do not suddenly stop taking Zismirt orotab, even when your depression has lifted. If you suddenly stop taking Zismirt orotab you may feel sick, dizzy, agitated or anxious, and have headaches. These symptoms can be avoided by stopping gradually. Your doctor will tell you how to decrease the dose gradually.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following happen, stop taking Zismirt orotab and tell your doctor immediately or go to the casualty department at your nearest hospital:

Rare (may affect up to 1 in 1,000 people)
- inflammation of the pancreas. This causes moderate to severe pain in the stomach, which spreads to the back.

Not known (cannot be estimated from the available data)
- epileptic attack (convulsions)
- yellow colouring of eyes or skin; this may suggest disturbance in liver function (jaundice)
- a combination of symptoms such as fever, sweating, increased heart rate, diarrhoea, (uncontrollable) muscle contractions, shivering, overactive reflexes, restlessness, mood changes and unconsciousness. In very rare cases these can be signs of serotonin syndrome.
- thoughts of harming or killing yourself or attempting to kill yourself

- reddish patches on the trunk which are target-like macules or circular, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis).
- widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).
- signs of infection such as sudden high fever, sore throat and mouth ulcers (agranulocytosis). Mirtazapine can cause disturbances in the production of blood cells (bone marrow depression). Some people become less resistant to infection because mirtazapine can cause a temporary shortage of white blood cells (granulocytopenia). In rare cases mirtazapine can also cause a shortage of red and white blood cells, as well as blood platelets (aplastic anemia), a shortage of blood platelets (thrombocytopenia) or an increase in the number of white blood cells (eosinophilia)
- breakdown of muscle tissue, causing muscle pain, tenderness, stiffness and/or weakness and darkening or discolouration of the urine (rhabdomyolysis)
- difficulty passing urine or emptying the bladder
- a lower than normal level of sodium in the blood, which may make you feel weak and confused with aching of muscles. This may be due to inappropriate ADH secretion, a hormone that causes the body to retain water and dilute the blood, reducing the amount of sodium.

Other possible side effects

Very common (may affect more than 1 in 10 people)
- increase in appetite or weight gain
- drowsiness or sleepiness
- headache
- dry mouth

Common (may affect up to 1 in 10 people)
- lethargy
- dizziness
- shakiness or tremor
- feeling sick (nausea)
- diarrhoea
- being sick (vomiting)
- constipation
- rash or skin eruptions (exanthema)
- pain in your joints (arthralgia) or muscles (myalgia)
- back pain
- feeling dizzy or faint when you stand up suddenly (orthostatic hypotension)
- swelling (typically in ankles or feet) caused by fluid retention (oedema)
- tiredness
- vivid dreams
- confusion
- feeling anxious
- sleeping problems
- memory problems, which in most cases resolved when treatment was stopped

Uncommon (may affect up to 1 in 100 people)
- feeling elated or emotionally ‘high’ (mania)
- abnormal sensation in the skin e.g. burning, stinging, tickling or tingling (paraesthesia)
- restless legs
- fainting (syncope)

- sensations of numbness in the mouth (oral hypoaesthesia)
- low blood pressure
- nightmares
- feeling agitated
- seeing, feeling or hearing things that are not there (hallucinations)
- urge to move

Rare (may affect up to 1 in 1,000 people)
- muscle twitching or contractions (myoclonus)
- aggressive behaviour
- increased liver enzymes, seen in a blood test

Not known: frequency cannot be estimated from the available data
- abnormal sensations in the mouth e.g. burning, stinging, tickling or tingling (oral paraesthesia)
- swelling in the mouth (mouth oedema)
- low sodium levels in the blood (hyponatraemia), seen in a blood test
- increased creatine kinase blood levels, seen in a blood test
- increased salivation
- sleep walking
- difficulty in speaking
- increased prolactin hormone levels in blood (hyperprolactinemia, including symptoms of enlarged breasts and/or milky nipple discharge)
- prolonged painful erection of the penis

Additional side effects in children and adolescents
In children under 18 years the following adverse events were observed commonly in clinical trials: hives and increased blood triglycerides.

Reporting side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance. Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zismirt orotab

Keep this medicine out of the sight and reach of children.

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

This medicinal product does not require any special storage conditions.

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 protect the environment.

6. Contents of the pack and other information

What Zismirt orotab contains

- The active substance is mirtazapine.
  Each orodispersible tablet contains 15 mg mirtazapine.
  Each orodispersible tablet contains 30 mg mirtazapine.
  Each orodispersible tablet contains 45 mg mirtazapine.
- The other ingredients are: crospovidone, mannitol, microcrystalline cellulose, aspartame (see section 2 'Zismirt orotab contains aspartame'), strawberry guarana flavour, peppermint flavour, colloidal anhydrous silica and magnesium stearate.

What Zismirt orotab looks like and contents of the pack

Zismirt orotab 15 mg orodispersible tablets are round, white tablets marked with 'A' on one side and marked '36' on the other side.
Zismirt orotab 30 mg orodispersible tablets are round, white tablets marked with 'A' on one side and marked '37' on the other side.
Zismirt orotab 45 mg orodispersible tablets are round, white tablets marked with 'A' on one side and marked '38' on the other side.

Zismirt orotab is available in blister packs containing: 6, 12, 18, 30, 48, 60, 90, 96 and 100 orodispersible tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
McDermott Laboratories Ltd. t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.

Manufacturers
McDermott Laboratories Ltd. t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.
Mylan Hungary Kft, H-2900 Komárom, Mylan utca 1, Hungary.

This medicinal product is authorised in the Member States of the EEA and in the United Kingdom (Northern Ireland) under the following names:

Czech Republic	Mirtazapin Mylan
Denmark	Mirtazapin Mylan
Ireland	Zismirt orotab 15 mg, 30 mg & 45 mg orodispersible tablets
Italy	Mirtazapina Mylan Generics Italia
Poland	Mirtagen
Portugal	Mirtazapina Mylan
Spain	Mirtazapina Flas Viatris 15 mg & 30 mg comprimidos bucodispersables EFG
The Netherlands	Mirtazapine SmeltTab Mylan 15 mg, 30 mg & 45 mg orodispergeerbare tablet
United Kingdom (Northern Ireland)	Mirtazapine 15 mg, 30 mg & 45 mg orodispersible tablets

This leaflet was last revised in 11/2022.