Package Leaflet: Information for the patient

Zismirt 30mg Film-coated 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 is and what it is used for

Zismirt is one of a group of medicines called antidepressants. Zismirt is used to treat depressive illnesses.

2. What you need to know before you take Zismirt

Do not take Zismirt
- 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 (MAOIs).

Warnings and precautions

Do not take or tell your doctor before taking Zismirt:
If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Zismirt 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. 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 should not be restarted.

Children and adolescents under 18 years of age
Zismirt should normally not be used for children and adolescents under 18 years because efficacy has not been 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 medicines. Despite this, your doctor may prescribe Zismirt for patients under 18 because he/she decides that this is in their best interests. If the doctor has prescribed Zismirt 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. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Zismirt 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 Mirtazapine 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 Mirtazapine if you have, or have ever had one of the following conditions.

Tell your doctor about these conditions before taking Zismirt, if not done previously
- **seizures** (epilepsy);
- **liver disease**, including jaundice;
- **kidney disease;**
- **heart disease** or **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.

During treatment
- if you develop signs of infection such as inexplicable high fever, sore throat and mouth ulcers. In rare cases these symptoms can be signs of disturbances in blood cell production in the bone marrow. While rare, these symptoms most commonly appear after 4-6 weeks of treatment.
- if you are an older person. You could be more sensitive to the side effects of antidepressants.

Other medicines and Zismirt

Do not take Zismirt in combination with:
monoamine oxidase inhibitors (MAO inhibitors). Also, do not take Zismirt during the two weeks after you have stopped taking an MAO inhibitors. If you stop taking Zismirt, 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** e.g. sumatriptan (used to treat migraine), 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 alone or the combination of Zismirt with these medicines, can lead to a so-called serotonin syndrome. Some of the signs of this syndrome are: inexplicable 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**;

- **the antidepressant nefazodone**. It can increase the amount of Zismirt in your blood. Inform your doctor if you are using this medicine. It might be needed to lower the dose of Zismirt, or when use of nefazodone is stopped, to increase the dose of Zismirt again.
- **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 Zismirt can increase the drowsiness caused by these medicines.
- **medicines for infections**, medicines for bacterial infections (such as erythromycin), medicines for fungal infections (such as ketoconazole) and medicines for HIV/AIDS (such as HIV-protease inhibitors e.g. ritonavir, nelfinavir).
- **Cimetidine**, medicines for stomach ulcers. In combination with Zismirt 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, or when these medicines are stopped, to increase the dose of Zismirt again.
- **carbamazepine and phenytoin**, medicines for epilepsy
- **medicines for tuberculosis** such as rifampicin.
- In combination with Zismirt 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, or when these medicines are stopped to lower your dose of Zismirt again.
- **warfarin**, medicine to prevent blood clotting. Zismirt 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.
- **medicines that may affect the heart's rhythm** such as certain antibiotics and some anti-psychotics.

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

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

Pregnancy
Limited experience with Zismirt administration to pregnant women does not indicate an increased risk. However, caution should be exercised when used during pregnancy.
If you use Zismirt until, or shortly before birth, your baby should be monitored for possible adverse effects.

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

Breast-feeding
Zismirt passes into breast milk in small amounts. There is a potential risk of an effect on the baby. Therefore, you should discuss the matter with your doctor, and he/she will decide whether you should stop breast-feeding or stop the therapy with Zismirt.

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

Zismirt contains lactose
If you have been told by your doctor that you have an intolerance for some sugars, such as lactose, contact your doctor before taking this medicine.

3. How to take Zismirt

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
Adults:
The recommended starting 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 older person or if you have kidney or liver disease, your doctor may change the dose.

The score line is only there to help you break the tablet if you have difficulty swallowing it whole.

When can you expect to start feeling better
Usually Zismirt 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:
2 to 4 weeks after you have started taking Zismirt, 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 until your symptoms of depression have disappeared for 4 to 6 months.

Use in children and adolescents under the age of 18 years:
Zismirt 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").

When to take Mirtazapine
Take Mirtazapine at the same time each day. It is best to take Mirtazapine as a single dose before you go to bed. However your doctor may suggest you to split your dose of Mirtazapine – 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.
Swallow your tablets without chewing, with some water or juice.

If you take more Zismirt than you should
If you or someone else have taken too much Zismirt, call a doctor straight away**.** The most likely signs of an overdose of Zismirt (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
If you are supposed to take your dose **once a day**
- if you have forgotten to take your dose of Zismirt, 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
Only stop taking Zismirt 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, even when your depression has lifted. If you suddenly stop taking Zismirt 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.
In some cases the side effect is not caused by the medicine but is a sign of your illness.

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

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.
- yellowing of your skin or eyes; this may suggest disturbance in liver function (jaundice).

Not known (cannot be estimated from the available data)
- serious allergic reactions such as rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing.
- 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). Mirtazapine can also cause a shortage of red and white blood cells which may cause pale skin, feeling tired and breathless and having dark urine, blood platelets (aplastic anaemia), a shortage of blood platelets with signs of bleeding or bruising more easily than normal (thrombocytopenia) or an increase in the number of white blood cells (eosinophilia).
- 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.
- thoughts of harming or killing yourself (see section 2 “Thoughts of suicide and worsening of your depression”).
- epileptic attack (convulsions).
- a combination of symptoms such as inexplicable fever, sweating, increased heart rate, diarrhoea, (uncontrollable) muscle contractions, shivering, overactive reflexes, restlessness, mood changes and unconsciousness. These can be signs of serotonin syndrome.
- signs of severe skin reaction or disease which may include rash, red skin, fever, sore throat, and fatigue, which may be followed by ulcers, peeling of the skin and other lesions, usually around the mouth and lips (Stevens-Johnson syndrome, toxic epidermal necrolysis, dermatitis bullous or erythema multiforme).
- widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).
- 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.

Other possible side effects

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

Common (may affect up to 1 in 10 people)
- lethargy
- dizziness
- shakiness or tremor
- nausea
- diarrhoea
- 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)
  Stop taking Zismirt and tell your doctor straight away.
- 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 (cannot be estimated from the available data)
- abnormal sensations in the mouth (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
- difficulty speaking
- increased salivation
- sleepwalking

- 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: significant weight gain, hives and increased blood triglycerides.

Reporting of 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

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 or container after EXP. The expiry date refers to the last day of that month.

Store in the original package.

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 contains
The active substance is mirtazapine. Each tablet contains 30 mg of mirtazapine.

The other ingredients are anhydrous lactose (see section 2 “Mirtazapine contains lactose”), maize starch, colloidal anhydrous silica, hydroxypropyl cellulose low substituted and magnesium stearate. The coating includes titanium dioxide (E171), macrogol 4000, lactose monohydrate (see section 2 “Mirtazapine contains lactose”), red iron oxide (E172), yellow iron oxide (E172), black iron oxide (E172) and hypromellose.

What Zismirt looks like and contents of the pack
Your medicine comes as a round film-coated tablet. The tablets are buff-coloured, marked ‘MR|30’on one side and ‘G’ on the other.
Zismirt is available in blisters packs and plastic containers of 10, 14, 20, 28, 30, 50, 100, 250 and 500 film-coated tablets. Not all pack sizes may be marketed.

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

Manufacturer
Mylan Hungary Kft, Mylan utca 1., Komárom, 2900, Hungary.
McDermott Laboratories t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.
Mylan B.V., Krijgsman 20, 1186 DM Amstelveen, The Netherlands.

This medicin is authorised in the Member States of the European Econimic Area and in the United Kingdom (Northern Ireland) under the following names:

Belgium	Mirtazapine Viatris 15mg, 30mg, 45mg filmomhulde tabletten
Germany	Mirtazapin dura 15mg, 30mg, 45mg Filmtabletten
Greece	MIRTAZAPINE/MYLAN F.C. TAB 30 mg/TAB, 45mg/TAB
Ireland	Zismirt 30mg Film-coated tablets
Italy	Mirtazapina Mylan Generics 30mg, 45mg
The Netherlands	Mirtazapine Mylan 15mg, 30mg, 45mg filmomhulde tabletten
Portugal	Mirtazapina Mylan
Spain	Mirtazapina Viatris Pharmaceuticals 30 mg comprimidos recubiertos con película EFG
United Kingdom (Northern Ireland)	Mirtazapine 30mg Film-coated tablets

This leaflet was last revised in February 2023.