Package Leaflet: Information for the user

BY-MADOL SR 200 mg prolonged-release capsules, hard

Tramadol hydrochloride

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What By-Madol SR is and what it is used for

Tramadol hydrochloride – the active substance of By-Madol SR –belongs to a group of medicines known as opioid analgesics or painkillers. Its pain-relieving action is due to its effect on specific nerve cells in the spinal cord and brain.

By-Madol SR is used in the treatment of moderate to severe pain.

2. What you need to know before you take By-Madol SR

Do not take By-Madol SR:
- if you are allergic to tramadol or any of the other ingredients of this medicine (listed in section 6).
- if you are intoxicated with alcohol or with sedative drugs include sleeping pills, other painkillers or psychotropic medicines (medicines that affect mood and emotions)
- if you are taking, or have taken in the last two weeks, certain medicines called "monoamine oxidase inhibitors" or MAOIs (used to treat depression). The combination could result in a serious, potentially life threatening interaction (see "Other medicines and By-Madol SR")
- if you have epilepsy that is not controlled with your current medicine

By-Madol SR is not suitable as a drug substitute for the treatment of drug addiction.

By-Madol SR is contraindicated in children below 12 years of age.

Warnings and Precautions
Talk to your doctor, pharmacist or nurse before taking By-Madol SR;

- if you think that you are addicted to other pain relievers (opioids);
- if you suffer from consciousness disorders (if you feel that you are going to faint);
- if you are in a state of shock (cold sweat may be a sign of this);
- if you suffer from epilepsy or seizures (fits) or have had them in the past, because tramadol could increase the risk of you having further fits;
- If you suffer from depression and you are taking antidepressants as some of them may interact with tramadol (see 'Other medicines and By-Madol SR')
- if you have liver or kidney problems;
- if you experience extreme fatigue, lack of appetite, severe abdominal pain, nausea, vomiting or low blood pressure. This may indicate that you have adrenal insufficiency (low cortisol levels). If you have these symptoms, contact your doctor, who will decide if you need to take hormone supplement;

Sleep-related breathing disorders
Tramadol can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

Tramadol is transformed in the liver by an enzyme. Some people have a variation of this enzyme and this can affect people in different ways. In some people, they may not get enough pain relief but other people are more likely to get serious side effects. If you notice any of the following side effects, you must stop taking this medicine and seek immediate medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, lack of appetite.

Epileptic fits have been reported in patients taking tramadol at the recommended dose level. The risk may be increased when doses of tramadol exceed the recommended upper daily dose limit (400 mg).

As with all opioids, tramadol should be used with caution, and only under medical supervision in seriously ill patients including those with impaired breathing, excessively low blood pressure (shock), serious head injury or brain diseases that may cause elevated pressure in the skull.

As with all opioids, tramadol may lead to psychological and physical dependence or addiction in some people, especially with long term use. The dose needed to achieve the desired effect may increase with time. Tramadol should be used with caution, and only for short periods, in patients who are addicted to other opioid pain-killers.

There is a small risk that you may experience a so-called serotonin syndrome that can occur after having taken tramadol in combination with certain antidepressants or tramadol alone. Seek medical advice immediately if you have any of the symptoms related to this serious syndrome (see section 4 'Possible side effects').

Children and adolescents
Use in children with breathing problems

Tramadol is not recommended in children with breathing problems, since the symptoms of tramadol toxicity may be worse in these children.

Other medicines and Tramadol Ethypharm
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

The pain-relieving effect of By-Madol SR may be weakened and/or shortened if you also take medicines containing:

- carbamazepine (used to treat epilepsy)
- pentazocine, nalbuphine or buprenorphine (pain killers)
- ondansetron (used to stop you feeling sick).

Your doctor will tell you whether you should take By-Madol SR, and which dose.

The risk of side effects increases,
- if you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk having a fit may increase if you take By-Madol SR at the same time. Your doctor will tell you whether By-Madol SR is suitable for you.
- if you are taking certain antidepressants. By-Madol SR may interact with these medicines and you may experience serotonin syndrome (see section 4 'Possible side effects').
- if you take By-Madol SR at the same time as sedative medicines such as tranquillizers or sleeping pillsand other pain relievers (morphine, codeine – also as cough medicine). You may feel excessively drowsy or feel that you might faint. If it happens tell your doctor.
- if you take By-Madol SR at the same time as alcohol. Tramadol may increase the intoxicating effect of alcohol and therefore you should be cautious if you wish to drink alcohol during treatment with By-Madol SR.
- if you take By-Madol SR at the same time as medicines that inhibit blood clotting, such as warfarin. The dose of these medicines may need to be reduced, otherwise there could be an increased risk of potentially serious bleeding.

Do not take By-Madol SR at the same time as medicines called "monoamine oxidase inhibitors" (which are used to treat depression), or if you have taken one in the past 2 weeks.

Concomitant use of By-Madol SR and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.
However if your doctor does prescribe By-Madol SR together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.
Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

By-Madol SR with food and alcohol
Do not drink alcohol during treatment with By-Madol SR as its effect may be intensified.
Food does not influence the effect of By-Madol SR.

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

By-Madol SR may affect an unborn child. Therefore it should not be taken during pregnancy.

Tramadol is excreted into breast milk. For this reason, you should not take By-Madol SR more than once during breast-feeding, or alternatively, if you take By-Madol SR more than once, you should stop breast-feeding.

Based on human experience tramadol is suggested not to influence female or male fertility.

Driving and using machines

By-Madol SR may cause side effects such as drowsiness and blurred vision. If this happens, do not drive or use any tools/ machines and do not perform any hazardous tasks.

By-Madol SR contains sucrose and benzoic acid
This medicine contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
This medicine contains less than 0.015 mg of benzoic acid in each dosage unit.

3. How to take By-Madol SR

The dosage should be adjusted to the intensity of your pain and your individual pain sensitivity.
In general the lowest pain-relieving dose should be taken.

Always take By-Madol SR exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual doses are given below. Your doctor may gradually increase or decrease your dose depending on how you respond to the treatment.

Adults and adolescents aged 12 and over:
The usual dose is one to two 100mg-capsules taken twice a day, equivalent to 200 to 400 mg per day. The capsules should be taken in the morning and evening. You should not normally take more than 400 mg a day.

Use in children:
This medicinal product is not suitable for use in children below 25 kg body weight which in general does not allow for individualized dosage in children below 12 years of age. Other form(s) of this medicine may be more suitable for children; ask your doctor, pharmacist or nurse.

Elderly patients:
In elderly patients (above 75 years) the excretion of tramadol may be delayed. If this applies to you, your doctor may recommend prolonging the dosage interval.

Severe liver or kidney disease (insufficiency)/dialysis patients:
Patients with severe liver and/or kidney problems, should not take By-Madol SR.
If in your case the insufficiency is mild or moderate, your doctor may may recommend prolonging the dosage interval.

Route and method of administration
For oral use.
The capsules should be swallowed whole with a glass of water.
The capsules can be taken with or without food. They should NOT be chewed, divided or crushed.

How long should you take By-Madol SR
You should not take By-Madol SR for longer than necessary. If you need to be treated for a longer period, your doctor will check at regular short intervals (if necessary with breaks in treatment) whether you should continue to take By-Madol SR and at what dose.
If you have the impression that the effect of By-Madol SR is too strong or too weak, talk to your doctor or pharmacist.

If you take more By-Madol SR than you should
If high doses are taken accidentally, you should contact your doctor immediately or go to your nearest hospital casualty department. A number of symptoms may occur.

These might include: very small pupils, vomiting (being sick), a fall in blood pressure, a fast heartbeat, collapse, fainting or even coma, epileptic fits and difficulties in breathing or shallow breathing.

If you forget to take By-Madol SR, take it as soon as you remember and then carry on as before. Do not take a double dose to make up for a forgotten dose.

If you stop taking By-Madol SR, your pain may return.
You should not suddenly stop taking this medicine unless your doctor tells you to. If you want to stop taking your medicine, discuss this with your doctor first, particularly if you have been taking it for a long time. Your doctor will advise you when and how to stop, which may be by lowering the dose gradually to reduce the chance of developing unnecessary side effects (withdrawal symptoms).

If you have been taking this medicine for a very long time, you may get the following side effects if you suddenly stop treatment: restlessness, anxiety, nervousness, shaking or an upset stomach. Very few people may get panic attacks, hallucinations, unusual perceptions such as itching, tingling and numbness, and "ringing" in the ears (tinnitus). Further unusual CNS symptoms, i.e. confusion, delusions, change of perception of the own personaility (depersonalisation), and change in perception of reality (derealisation) and delusion of persecution (paranoia) have been seen very rarely. If you get any of these effects after stopping treatment with By-Madol SR please talk to your doctor.

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

4. Possible side effects

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

By-Madol SR can occasionally cause allergic reactions although serious allergic reactions (including anaphylaxis and angioedema) are rare. Tell your doctor immediately if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

The following side effects may occur:

Very common: may affect more than 1 in 10 people

- Feeling sick (nausea)
- Dizziness

Common: may affect up to 1 in 10 people

- Headache
- Being sick (vomiting)
- Constipation
- Fatigue (tiredness)
- Drowsiness
- Dry mouth
- Sweating (hyperhidrosis)

Uncommon: may affect up to 1 in 100 people

- Effects on the heart and blood circulation (pounding of the heart, fast heartbeat, feeling faint or collapse). These adverse effects may particularly occur in patients in an upright position or under physical strain.
- Urge to be sick (retching)
- Stomach trouble (e.g.feeling pressure in the stomach, bloating, diarrhoea)
- Skin reactions (e.g. itchiness, rash, sudden onset of skin redness)

Rare: may affect up to 1 in 1,000 people

- Slow heartbeat
- Psychological complaints may appear

- Increased in blood pressure
- Changes in appetite
- Abnormal sensations (e.g. pins and needles, numbness), trembling, epileptic fits, muscle twitches, uncoordinated movement, transient loss of consciousness (syncope), speech disorders
- Slow breathing, shortness of breath (dyspnoea)
- Epileptic ("fits") have occurred mainly at high doses of tramadol or when tramadol was taken at the same time as other medicines which may induce fits.

after treatment with By-Madol SR. Their intensity and nature may vary (according to the patient's personality and length of therapy). These may appear as a change in mood (mostly high spirits, occasionally irritated mood), changes in activity (slowing down but sometimes an increase in activity) and decreased cognitive and sensory perception (being less aware and less able to make decisions, which may lead to errors in judgement).

- Hallucinations, confusion, sleep disorders, delirium, anxiety and nightmares
- Blurred vision, excessive dilation of the pupils (mydriasis), constriction of the pupil (miosis)
- Weak muscles
- Passing less urine than normal (dysuria) or passing urine with difficulty or pain
- Drug dependence may occur
- Psychological complaints may appear after treatment with By-Madol SR. Their intensity and nature may vary (according to the patient's personality and length of therapy). These may appear as a change in mood (mostly high spirits, occasionally irritated mood), changes in activity (slowing down but sometimes an increase in activity) and decreased cognitive and sensory perception (being less aware and less able to make decisions, which may lead to errors in judgement).
- Worsening of asthma has been reported, however it has not been established whether it was caused by tramadol. If the recommended doses are exceeded, or if other medicines that depress brain function are taken at the same time, breathing may slow down.
- Allergic reactions (e.g. difficulty in breathing, wheezing, swelling of skin) and shock (sudden circulation failure) have occurred in very rare cases.

Very rare: may affect up to 1 in 10,000 people

- Increased levels of liver enzymes

Not known:frequency cannot be estimated from the available data

- Decrease in blood sugar level (hypoglycaemia)
- Hiccups

- Serotonin syndrome, that can manifest as mental status changes (e.g. agitation, hallucinations, coma), and other effects, such as fever, increase in heart rate, unstable blood pressure, involuntary twitching, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) (see section 2 'What you need to know before you take By-Madol SR').

When treatment is stopped abruptly, signs of withdrawal may appear (see "If you stop taking By-Madol SR").

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website www.hpra.ie, e-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store By-Madol SR

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 blister and the carton after EXP. The expiry date refers to the last day of that month.

Do not store above 25°C.

Do not throw away any medicines via wastewater of household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What By-Madol SR contains
- The active substance is tramadol hydrochloride. Each capsule contains 200 mg of tramadol hydrochloride equivalent to 175.64 mg tramadol.
- The other ingredients are:

Sugar spheres (maize starch and sucrose)
Macrogol 4000
Polyacylate dispersion 30% (ethyl acrylate, methyl methacrylate, nonoxynol)
Simethicone emulsion (simethicone, polyoxyethylene sorbitan tristearate, methylcellulose, polyethylene glycol stearate, glycerides, xanthan gum, benzoic acid, sorbic acid, sulfuric acid)Hypromellose
Talc
Gelatin
Titanium dioxide (E 171)
Yellow iron oxide (E172).

What By-Madol SR looks like and contents of the pack
Opaque yellow cap and opaque white body gelatin capsules containing white spherical microgranules ("beads")
Pack sizes: 10, 20, 28, 30, 50, 56, 60, 100 capsules
Hospital packs: 500 capsules

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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This medicinal product is authorised in the Member States of the EEA under the following names:
Germany: Tramadol Ethypharm 200 mg
Ireland: By-Madol SR 200 mg
Portugal: Gelotralib 200 mg
Spain: ~~Gelotradol~~ Captor Simplex 200 mg
United-Kingdom: Maxitram SR 200 mg

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