Package leaflet: Information for the user

MISABRI PR 82.5 mg prolonged-release tablets
MISABRI PR 165 mg prolonged-release tablets
MISABRI PR 330 mg prolonged-release tablets
pregabalin

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 Misabri PR is and what it is used for

Misabri PR belongs to a group of medicines used to treat neuropathic pain in adults.

Misabri PR is used to treat long lasting pain caused by damage to the nerves. A variety of diseases can cause peripheral neuropathic pain, such as diabetes or shingles. Pain sensations may be described as hot, burning, throbbing, shooting, stabbing, sharp, cramping, aching, tingling, numbness, pins and needles. Peripheral and central neuropathic pain may also be associated with mood changes, sleep disturbance, fatigue (tiredness), and can have an impact on physical and social functioning and overall quality of life.

2. What you need to know before you take Misabri PR

Do not take Misabri PR
If you are allergic to pregabalin or any of the other ingredients of this medicine (listed in section 6).

Warnings and Precautions
Talk to your doctor or pharmacist before taking Misabri PR.

- Some patients taking Misabri PR have reported symptoms suggesting an allergic reaction. These symptoms include swelling of the face, lips, tongue, and throat, as well as diffuse skin rash. Should you experience any of these reactions, you should contact your physician immediately.
- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with pregabalin. Stop using this medicine and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

- Pregabalin, the active ingredient in Misabri PR has been associated with dizziness and somnolence, which could increase the occurrence of accidental injury (fall) in elderly patients. Therefore, you should be careful until you are used to any effect the medicine might have.
- This medicine may cause blurring or loss of vision, or other changes in eyesight, many of which are temporary. You should immediately tell your doctor if you experience any changes in your vision.
- Some patients with diabetes who gain weight while taking pregabalin may need an alteration in their diabetic medicines.
- Certain side effects may be more common, such as sleepiness, because patients with spinal cord injury may be taking other medicines to treat, for example, pain or spasticity, that have similar side effects to pregabalin and the severity of these effects may be increased when taken together.
- There have been reports of heart failure in some patients when taking pregabalin; these patients were mostly elderly with cardiovascular conditions. **Before taking this medicine you should tell your doctor if you have a history of heart disease**.
- There have been reports of kidney failure in some patients when taking pregabalin. If while taking this medicine you notice decreased urination, you should tell your doctor as stopping the medicine may improve this.
- Some patients being treated with anti-epileptics such as pregabalin have had thoughts of harming or killing themselves or shown suicidal behaviour. If at any time you have these thoughts or shown such behaviour, immediately contact your doctor.
- When this medicine is taken with other medicines that may cause constipation (such as some types of pain medicines) it is possible that gastrointestinal problems may occur (e.g. constipation, blocked or paralysed bowel). Tell your doctor if you experience constipation, especially if you are prone to this problem.
- Before taking this medicine you should tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines or illegal drugs; it may mean you have a greater risk of becoming dependent on this medicine.
- There have been reports of convulsions when taking pregabalin or shortly after stopping the treatment. If you experience a convulsion, contact your doctor immediately.
- There have been reports of reduction in brain function (encephalopathy) in some patients taking pregabalin when they have other conditions. Tell your doctor if you have a history of any serious medical conditions, including liver or kidney disease.
- There have been reports of breathing difficulties. If you have nervous system disorders, respiratory disorders, renal impairment, or you are older than 65, your doctor may prescribe you a different dosing regimen. Contact your doctor if you experience trouble breathing or shallow breaths.

<u>Dependence</u>

Some people may become dependent on pregabalin (a need to keep taking the medicine). They may have withdrawal effects when they stop using this medicine (see section 3, “How to take Misabri PR” and “If you stop taking Misabri PR”). If you have concerns that you may become dependent on this medicine, it is important that you consult your doctor.

If you notice any of the following signs whilst taking Misabri PR, it could be a sign that you have become dependent:

- You need to take the medicine for longer than advised by your prescriber

- You feel you need to take more than the recommended dose
- You are using the medicine for reasons other than prescribed
- You have made repeated, unsuccessful attempts to quit or control the use of the medicine
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again

If you notice any of these, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to do this safely.

Children and adolescents

The safety and efficacy in children and adolescents (under 18 years of age) has not been established and therefore, pregabalin should not be used in this age group.

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

Misabri PR and certain other medicines may influence each other (interaction). When taken with certain other medicines which have sedative effects (including opioids), Misabri PR may potentiate these effects, and could lead to respiratory failure, coma and death. The degree of dizziness, sleepiness and decreased concentration may be increased if Misabri PR is taken together with medicines containing:

- Oxycodone – (used as a pain-killer)
- Lorazepam – (used for treating anxiety)
- Alcohol

Misabri PR may be taken with oral contraceptives.

Misabri PR with food, drink and alcohol
You should not drink alcohol while taking Misabri PR. For information regarding treatment with Misabri PR in relation with food see section 3, “How to take Misabri PR”.

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.

This medicine should not be taken during pregnancy or when breast-feeding, unless you are told otherwise by your doctor. Pregabalin use during the first 3 months of pregnancy may cause birth defects in the unborn child that require medical treatment. In a study reviewing data from women in Nordic countries who took pregabalin in the first 3 months of pregnancy, 6 babies in every 100 had such birth defects. This compares to 4 babies in every 100 born to women not treated with pregabalin in the study. Abnormalities of the face (orofacial clefts), the eyes, the nervous system (including the brain), kidneys and genitals have been reported.

Effective contraception must be used by women of childbearing potential.

Driving and using machines
Misabri PR may produce dizziness, sleepiness and decreased concentration. You should not drive, operate complex machinery or engage in other potentially hazardous activities until you know

whether this medicine affects your ability to perform these activities.

3. How to take Misabri PR

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

Misabri PR is for oral use only. You should take Misabri PR once a day, in the evening, directly after an evening meal. Swallow the tablet whole with water. Do not split, crush or chew the tablet. The tablet should not be broken because this could impact its characteristics.

Your doctor will determine what dose is appropriate for you.

- Take the number of tablets as instructed by your doctor.
- The dose, which has been adjusted for you and your condition, will generally be between 165 mg and 660 mg each day.

If you have the impression that the effect of Misabri PR is too strong or too weak, talk to your doctor or pharmacist.

If you are an elderly patient (over 65 years of age), you should take this medicine normally, except if you have problems with your kidneys.
Your doctor may prescribe a different dosing schedule and/or dose if you have problems with your kidneys.

Continue taking Misabri PR until your doctor tells you to stop.

Switching from pregabalin immediate release medicines to pregabalin prolonged release medicines, like Misabri PR is:
When switching from pregabalin immediate release to pregabalin prolonged release, like this medicine, your doctor will instruct you how to do this. He will tell you to take the following steps:
- to take your morning dose of pregabalin immediate release as prescribed
- then start taking Misabri PR after an evening meal

Do not switch the medicines unless your doctor tells you to do so. He will also indicate the appropriate dosage for your condition.
If you have additional questions or you are not sure, talk with your doctor.

If you take more Misabri PR than you should
Call your doctor or go to the nearest hospital emergency unit immediately. Take your box or container (bottle) of Misabri PR tablets with you. You may feel sleepy, confused, agitated, or restless as a result of taking more Misabri PR than you should. Fits and unconsciousness (coma) have also been reported.

If you forget to take Misabri PR
It is important to take your Misabri PR tablets regularly at the same time each day. If you forget to take a dose, take it as soon as you remember, always after some food, unless it is time for your next dose. In that case, just carry on with the next dose as normal. Do not take a double dose to make up for a forgotten dose.

If you stop taking Misabri PR
Do not suddenly stop taking Misabri PR. If you want to stop taking this medicine, discuss this with your doctor first. They will tell you how to do this. If your treatment is stopped it should be done gradually. After stopping a short or long-term treatment with Misabri PR, you need to know that you may experience certain side effects, so-called withdrawal effects. These effects include, trouble

sleeping, headache, nausea, feeling anxious, diarrhoea, flu like symptoms, convulsions, nervousness, depression, thoughts of harming or killing yourself, pain, sweating, and dizziness. These effects may occur more commonly or severely if you have been taking Misabri PR for a longer period of time. If you experience withdrawal effects, you should contact your doctor.

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.

Very common: may affect more than 1 in 10 people

Dizziness, drowsiness, headache.

Common: may affect up to 1 in 10 people

- Increased appetite.
- Feeling of elation, confusion, disorientation, decrease in sexual interest, irritability.
- Disturbance in attention, clumsiness, memory impairment, loss of memory, tremor, difficulty with speaking, tingling feeling, numbness, sedation, lethargy, insomnia, fatigue, feeling abnormal.
- Blurred vision, double vision.
- Vertigo, problems with balance, fall.
- Dry mouth, constipation, vomiting, flatulence, diarrhoea, nausea, swollen abdomen.
- Difficulties with erection.
- Swelling of the body including extremities.
- Feeling drunk, abnormal style of walking.
- Weight gain.
- Muscle cramp, joint pain, back pain, pain in limb.
- Sore throat.

Uncommon: may affect up to 1 in 100 people

- Loss of appetite, weight loss, low blood sugar, high blood sugar.
- Change in perception of self, restlessness, depression, agitation, mood swings, difficulty finding words, hallucinations, abnormal dreams, panic attack, apathy, aggression, elevated mood, mental impairment, difficulty with thinking, increase in sexual interest, problems with sexual functioning including inability to achieve a sexual climax, delayed ejaculation.
- Changes in eyesight, unusual eye movement, changes in vision including tunnel vision, flashes of light, jerky movements, reduced reflexes, increased activity, dizziness on standing, sensitive skin, loss of taste, burning sensation, tremor on movement, decreased consciousness, loss of consciousness, fainting, increased sensitivity to noise, feeling unwell.
- Dry eyes, eye swelling, eye pain, weak eyes, watery eyes, eye irritation.
- Heart rhythm disturbances, increased heart rate, low blood pressure, high blood pressure, changes in heart beat, heart failure.

- Flushing, hot flushes.
- Difficulty breathing, dry nose, nasal congestion.
- Increased saliva production, heartburn, numb around mouth.
- Sweating, rash, chills, fever.
- Muscle twitching, joint swelling, muscle stiffness, pain including muscle pain, neck pain.
- Breast pain.
- Difficulty with or painful urination, incontinence.
- Weakness, thirst, chest tightness.
- Changes in blood and liver test results (blood creatinine phosphokinase increased, alanine amino transferase increased, aspartate aminotransferase increased, platelet count decreased, neutropaenia, increase in blood creatinine, decrease in blood potassium).
- Hypersensitivity, swollen face, itchiness, hives, runny nose, nose bleed, cough, snoring.
- Painful menstrual periods.
- Coldness of hands and feet.

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

- Abnormal sense of smell, swinging vision, altered perception of depth, visual brightness, vision loss.
- Dilated pupils, cross eyes.
- Cold sweat, tightness of the throat, swollen tongue.
- Inflammation of the pancreas.
- Difficulty in swallowing.
- Slow or reduced movement of the body.
- Difficulty with writing properly.
- Increased fluid in the abdomen.
- Fluid in the lungs.
- Convulsions.
- Changes in the recording of electrical changes (ECG) in the heart which correspond to heart rhythm disturbances.
- Muscle damage.
- Breast discharge, abnormal breast growth, breast growth in males.
- Interrupted menstrual periods.
- Kidney failure, reduced urine volume, urinary retention.
- Decrease in white blood cell count.
- Inappropriate behaviour, suicidal behaviour, suicidal thoughts.
- Allergic reactions which may include difficulty breathing, inflammation of the eyes (keratitis) and serious skin reactions characterized by reddish non-elevated, target-like or circular patches on the trunk, 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).

- Jaundice (yellowing of the skin and eyes).
- Parkinsonism, that is symptoms resembling Parkinson's disease; such as tremor, bradykinesia (decreased ability to move), and rigidity (muscle stiffness).

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

- Liver failure.
- Hepatitis (inflammation of the liver).

Not known: frequency cannot be estimated from the available data

- Becoming dependent on Misabri PR ('drug dependence').

After stopping a short or long-term treatment with this medicine, you need to know that you may experience certain side effects, so-called withdrawal effects (see "If you stop taking Misabri PR").If you experience swollen face or tongue or if your skin turns red and starts to blister or peel, you should seek immediate medical advice.

Certain side effects may be more common, such as sleepiness, because patients with spinal cord injury may be taking other medicines to treat, for example, pain or spasticity, that have similar side effects to Pregabalin and the severity of these effects may be increased when taken together.

The following adverse reaction has been reported in the postmarketing experience: Trouble breathing, shallow breaths.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Misabri PR

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 box or container (bottle). The expiry date refers to the last day of that month.

For 82.5 mg: Do not store above 30°C.
For 165 mg and 330 mg: This medicine 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 Misabri PR contains
The active substance is pregabalin. Each prolonged-release tablet contains either 82.5 mg, 165 mg or

330 mg of pregabalin.

The other ingredients are:
- Tablet core: hypromellose, hydroxypropyl cellulose (E 463), basic butylated methacrylate copolymer (E 1205), crospovidone (Type A), magnesium stearate (E 470b), silica colloidal anhydrous (E 551),
- Tablet coating: polyvinyl alcohol (E 1203), titanium dioxide (E 171), macrogol (E 1521) and talc (E 553b).
- The 165mg tablet also contains iron oxide yellow (E 172) and iron oxide red (E 172).
- The 330mg tablet also contains iron oxide red (E 172) and iron oxide black (E 172)
- Printing ink: shellac, iron oxide black (E 172), propylene glycol (E 1520)

What Misabri PR looks like and contents of the pack
Misabri PR 82.5 mg prolonged-release tablet
White, oval, unscored, blank on one side and imprinted "ALV 379" on the other side with black ink, with a length of 19 mm, a width of 12 mm and thickness of approximately 7 mm.

Misabri PR 165 mg prolonged-release tablet
Yellow, oval, unscored, blank on one side and imprinted "ALV 380" on the other side with black ink, with a length of 19 mm, a width of 12 mm and thickness of approximately 7 mm.

Misabri PR 330 mg prolonged-release tablet
Pink, oval, unscored, blank on one side and imprinted "ALV 381" on the other side with black ink, with a length of 19 mm, a width of 12 mm and thickness of approximately 8 mm.

Misabri PR is available in:
- Carton box containing white, wide-mouthed, round HDPE container (bottle) with child-resistant white cap with liner and one desiccant cylinder.
- Original pack with 30 prolonged-release tablets, multipack with 90 (3 x 30) prolonged- release tablets.

Not all pack sizes may be marketed.

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