

VI.2 Elements for a public summary

Part VI.2 "Elements for a public summary" is applicable for all products that are covered by this RMP, except from the important potential risk of "Medication error with pregabalin oral solution". Evidently this risk is applicable only for oral solution products.

VI.2.1 Overview of disease epidemiology

Neuropathic pain

Neuropathic pain is a chronic pain state that may result from disorders of the peripheral or the central nervous system (brain and spinal cord). With neuropathic pain, the nerve fibres themselves might be damaged, dysfunctional or injured. These damaged nerve fibres send incorrect signals to other pain centres. The impact of a nerve fibres injury includes a change in nerve function both at the site of injury and areas around the injury (WebMD 2013). Neuropathic pain may be associated with abnormal sensations. Common qualities include burning or coldness, "pins and needles" sensations, numbness and itching. Major causes of neuropathic pain include diabetes, shingles, spinal cord injury, stroke, multiple sclerosis, cancer, and HIV infection (Saeed 2010). Up to 7 % to 8 % of the European population is affected, and in 5 % of persons it may be severe (Bouhassira et al 2008, Torrance et al 2006).

Epilepsy

Epilepsy is a chronic brain disorder that affects people of all ages. It is characterized by recurrent brief episodes of involuntary shaking (seizures) which may involve a part of the body (partial) or the entire body (generalized) and sometimes accompanied by loss of consciousness and control of bowel or bladder function. The episodes are a result of excessive electrical discharges in a group of brain cells. Seizures can vary from the briefest lapses of attention or muscle jerks, to severe and prolonged convulsions. Seizures can also vary in frequency, from less than one per year to several per day. The estimated proportion of the general population with active epilepsy is between 4 to 10 per 1,000 people (in developing countries between 6 to 10 per 1,000). Around 50 million people in the world have epilepsy; nearly 80 % are found in developing regions (WHO 2014).

Generalised Anxiety Disorder

Generalized anxiety disorder is characterized by excessive and persistent worrying that is hard to control, causes significant distress or impairment, and occurs on more days than not for at least six months. Other features include psychological symptoms of anxiety, such as apprehensiveness and irritability, and physical (or somatic) symptoms of anxiety, such as increased fatigue and muscular tension (UpToDate 2014). The cause is believed to be related to both genetic and environmental factors. The number of people affected by this condition varies between different countries and cultures. (Yates WR 2014). In Europe, estimated 12-month prevalence is 1.7 % to 3.4 % and lifetime prevalence is 4.3 % to 5.9 % (UpToDate 2014).

VI.2.2 Summary of treatment benefits

Based on the available data from clinical studies and clinical experience of several years, pregabalin represents an effective drug indicated to treat adults with the following conditions:

- **Peripheral and central neuropathic pain:** Pregabalin 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 or 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.
- **Epilepsy:** Pregabalin is used to treat a certain form of epilepsy (partial seizures with or without secondary generalisation) in adults. Pregabalin is prescribed to help treat the epilepsy when the current treatment is not controlling the condition. Pregabalin should be taken in addition to the current treatment. Pregabalin is not intended to be used alone, but should always be used in combination with other anti-epileptic treatment.
- **Generalised Anxiety Disorder:** Pregabalin is used to treat Generalised Anxiety Disorder (GAD). The symptoms of GAD are prolonged excessive anxiety and worry that are difficult to control. GAD can also cause restlessness or feeling keyed up or on edge, being easily fatigued (tired), having difficulty concentrating or mind going blank, feeling irritable, having muscle tension or sleep disturbance. This is different to the stresses and strains of everyday life.

If administered as indicated in the Summary of Product Characteristics and taking into account the contra-indications, the warnings and precautions, pregabalin can be considered effective in the approved indications.

VI.2.3 Unknowns relating to treatment benefits

No data are available regarding efficacy of pregabalin in children and adolescents aged 12 to 17 years.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Weight gain	Pregabalin can cause weight gain. Some patients with diabetes who gain weight while taking pregabalin may need an alteration in their diabetic medicines.	Tell your doctor if you are taking, have recently taken or might take any other medicines. If you get any side effects, talk to your doctor or pharmacist.
Swelling (oedema) of the body, including in the extremities (peripheral oedema)	Some patients develop swelling of the body, including in the extremities.	If you get any side effects, talk to your doctor or pharmacist.
Dizziness, sleepiness, loss of consciousness, fainting (syncope), and potential for accidental injury	Pregabalin treatment has been associated with dizziness and sleepiness, which could increase the occurrence of accidental injury (e.g. fall) in elderly patients. There have also been reports of loss of consciousness, confusion and mental impairment.	You should be careful until you are used to any effect the medicine might have. 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. It is advised not to drink alcohol while taking pregabalin. Tell your doctor if you are taking, have recently taken or might take any other medicines.
Events after pregabalin discontinuation	After stopping long and short-term pregabalin treatment, some patients may experience certain side effects. These include trouble sleeping, headache, feeling sick (nausea), feeling anxious, diarrhoea, flu-like symptoms, convulsions, nervousness, depression, pain, sweating, and dizziness. These symptoms may occur more commonly or severely if the patient has been taking pregabalin for a longer period of time.	Do not stop taking pregabalin unless your doctor tells you to. If your treatment is stopped it should be done gradually over a minimum of 1 week.
Simultaneous use with lorazepam, alcohol or other medicine that effects central nervous system (drug interactions)	Pregabalin and certain other medicines may influence each other (interaction). When taken with certain other medicines, pregabalin may enhance the side effects seen with these medicines, including respiratory failure and coma. The degree of dizziness, sleepiness and decreased concentration may be increased if pregabalin is taken together with	Tell your doctor if you are taking, have recently taken or might take any other medicines. It is advised not to drink alcohol while taking pregabalin. Tell your doctor if you experience constipation, especially if you are prone to this problem.

Risk	What is known	Preventability
	medicinal products containing oxycodone (used as a pain-killer), lorazepam (used for treating anxiety) or alcohol.	
Elevated mood (euphoria)	Some patients treated with pregabalin could experience elevated mood.	Before taking this medicine you should tell your doctor if you have a history of alcoholism or drug dependence. Let your doctor know if you think you need more medicine than prescribed.
Hypersensitivity and allergic reactions	Some patients taking pregabalin have reported symptoms suggesting an allergic reaction. These symptoms include swelling of the face, lips, tongue, and throat, as well as diffuse skin rash.	Do not take the product if you are allergic to pregabalin or any of the other ingredients of this medicine. Should you experience any of these reactions, you should contact your doctor immediately.
Congestive heart failure	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.
Vision-related events	Pregabalin 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.
Abuse, misuse and drug dependence	Reports of abuse, misuse and drug dependence have been reported by patients. This has not been observed during clinical studies.	Before taking pregabalin, patients should tell their doctors if they have a history of alcoholism or drug dependence, or if they think they need more medicine than prescribed.

Important potential risks

Risk	What is known (including reason why it is considered a potential risk)
Cancer of the blood vessels (haemangiosarcoma)	Cancer of the blood vessels has been observed in mice exposed to pregabalin. There is no evidence of a similar risk in humans.
Thoughts of self-harming or suicide	A small number of people being treated with anti-epileptics such as pregabalin have had thoughts of harming or killing themselves. The cause of this is unknown. If patients have these thoughts while on pregabalin therapy, they should immediately contact their doctor.
Off label use in 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 these age groups.
Medication error with pregabalin oral solution	Pregabalin is removed from the body mainly by kidneys, and therefore, the risk of toxic reactions to pregabalin may be greater in patients with kidney problems. The dose should be adjusted in such patients. However, dosage adjustment based on kidney function may result in confusion leading to medication errors.

Missing information

Risk	What is known
Use in pregnant or breastfeeding women	<p>There are no adequate data on the use of pregabalin in pregnant women. Studies in animals have shown toxicity in the animal foetuses (reproductive toxicity) at high doses, but the potential risk for humans is unknown. Therefore, pregabalin should not be used during pregnancy unless the patients are told otherwise by their doctor. Effective contraception must be used by women of child-bearing potential.</p> <p>It is not recommended to breast-feed the baby while using pregabalin unless the patients are told otherwise by their doctor, as pregabalin is excreted into breast milk. The effect of pregabalin on newborns/infants is unknown.</p> <p>If patients are pregnant or breast-feeding, think they may be pregnant or are planning to have a baby, they should ask their doctor or pharmacist for advice before taking this medicine. The patients should ask their doctor or pharmacist for advice before taking any medicine while breast-feeding.</p>

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable.