VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Epilepsy is a long-term condition affecting the brain and is characterised by recurring seizures (or fits). It is one of the most common of diseases of the nervous system and every year about 50 new cases are diagnosed per 100,000 people in the population. For most patients there is no identifiable cause, though the condition can be caused by injury or damage to the brain as happens, for example, following strokes or in patients with brain tumours.

Neuropathic pain is pain that results from damage to nerve endings and it differs from other more common types of pain that are caused by injury or pressure to the surrounding tissues. Causes of neuropathic pain include diabetic neuropathy (nerve damage that occurs as a complication of diabetes), herpes zoster (shingles) and spinal-cord injury. The number of new cases diagnosed per 100,000 people has been estimated from a study conducted in the UK to be: 40 cases of pain after shingles, 27 cases of trigeminal neuralgia (a severe pain affecting the face) after nerve damage,1 case of limb pain after amputation, and 15 cases of pain after nerve damage from diabetes.

Generalised anxiety disorder is long-term anxiety or nervousness about everyday matters. The cause of generalised anxiety disorder is not clear although it is believed to be related to both genetic factors and life experiences.

The number of people affected by this condition varies between different counties and cultures.

Regardless of geography, however, women are more likely to be affected than men. There also appear to be more cases of generalised anxiety disorder among older people up until the age of 60, when the number of cases begins to decline. A study conducted in Norway found the combined estimate of the number of new cases of panic and generalised anxiety disorder to be 1.10 per 100,000 people per [*]

VI.2.2 Summary of treatment benefits

Pregabalin Pfizer has been compared with placebo (a dummy treatment) in 22 studies. In neuropathic pain, the benefits of Pregabalin Pfizer were evaluated for up to 12 weeks using a standard pain questionnaire. In 10 studies involving over 3,000 patients with peripheral neuropathic pain (either diabetic pain or shingles), 35% of the patients treated with Pregabalin Pfizer had a decrease in pain scores of 50% or more, compared with 18% of the patients treated with placebo. In a smaller study involving 137 patients with central neuropathic pain due to a spinal cord injury, 22% of patients treated with Pregabalin Pfizer had a decrease in pain scores of 50% or more, compared with 8% of the patients treated with placebo. In epilepsy, the benefits of Pregabalin Pfizer were evaluated in 3 studies involving 1,000 patients that looked at how much it reduced the number of seizures patients had after 11 to 12 weeks. About 45% of the patients taking 600 mg Pregabalin Pfizer a day and about 35% of those taking 300 mg Pregabalin Pfizer a day had a reduction in seizures of 50% or more. This compared with about 10% of the patients taking placebo. Pregabalin Pfizer was more effective than placebo in generalised anxiety disorder: in 8 studies involving over 3,000 patients, 52% of the patients taking Pregabalin Pfizer had an improvement of 50% or more in their anxiety measured with a standard anxiety questionnaire, compared with 38% of the patients taking placebo. [†]

VI.2.3 Unknowns relating to treatment benefits

There is a limited experience with Pregabalin administration to pregnant women. Therefore, capsules should not be used during pregnancy unless the benefits for the mother outweigh the possible risks to the foetus.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Hypersensitivity reactions, including allergic reactions	Some patients taking pregabalin have reported symptoms suggesting an allergic reaction. These symptoms include swelling of	Should patients experience any of these reactions, they should contact their physician immediately.

[*] Pregabalin EPAR. Summary of the risk management plan.EMA/247834/2014.Accessed on 04-July-2014. Available at : http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Risk-management-plan_summary/human/003880/WC500162272.pdf

[††] Pregabalin EPAR. Summary for the public.EMA/220635/2014.EMA/H/C/003880.Accessed on 04-July-2014 Available at : http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/003880/WC500166174.pdf

Risk	What is known	Preventability
	the face, lips, tongue, and throat, as well as diffuse skin rash.	
Dizziness, somnolence, loss of consciousness, syncope and for accidential injury	Pregabalin treatment has been associated with dizziness and sleepiness, which could increase the occurrence of accidental injury (e.g. falls) in the elderly population. There have also been post-marketing reports of loss of consciousness, confusion and mental impairment.	Patients should be advised to exercise caution until they are familiar with the potential effects of the medicine. Patients should not drive, operate complex machinery or engage in other potentially hazardous activities until they know whether the medicine affects their ability to perform these activities.
Events after pregabalin discontinuation (Withdrawal reaction)	After stopping long- and short-term pregabalin treatment, patients may experience certain side effects. These include, trouble sleeping, headache, nausea, feeling anxious, diarrhoea, flulike symptoms, convulsions, nervousness, depression, pain, sweating, and dizziness. It is not clear whether these symptoms occur more commonly or severely if patients have been taking pregabalin for a longer period of time.	Patients should not stop taking pregabalin unless their doctor tells them to. If treatment is to be stopped, it should be done gradually over a minimum of 1 week.
Congestive heart failure	There have been reports of heart failure in some patients when taking pregabalin; these patients were mostly elderly with pre-existingcardiovascular conditions.	Before taking this medicine patients should tell their doctor if they have a history of heart disease.
Weight gain	Some patients gain weight while being treated with pregabalin.	Some patients with diabetes who gain weight while taking pregabalin may need to alter their diabetes treatment.

Risk	What is known	Preventability
Periphal oedema and oedema-relevant events	Some patients develop swelling of the body, including extremities.	Patients should inform their doctor if they develop swelling.
Drug interactions (lorazepam, ethanol and CNS depressants)	Pregabalin and certain other medicines may< interact with each other. When taken with certain other medicines, pregabalin may potentiate (increase) 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 medicinal products containing oxycodon (used as a painkiller), lorazepam (used for treating anxiety) or alcohol.	Patients should tell their doctor or pharmacist if they are taking, have recently taken or might take any other medicines.
Euphoria	Some patients treated with pregabalin have experienced elevated mood.	Before taking pregabalin, patients should tell their doctor if they have a history of alcoholism or drug dependence. Patients should let their doctor know if they think they need more of the medicines than has been prescribed for them.
Vision related events (blurred vision)	pregabalin may cause blurring or loss of vision, or other changes in eyesight, many of which are temporary.	Patients should immediately tell their doctor if they experience any changes in vision.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Sucidality	A small number of patients being treated with anti-epileptics, including pregabalin, have shown a slightly increased risk of suicidal behaviour or thinking. The cause for this is unknown and a causal association with pregabalin has not been

Risk	What is known (Including reason why it is considered a potential risk)	
	suggested. If at any time patients have suicidal thoughts, they should immediately contact their doctor.	
Haemangiosarcoma (malignancy of vasculature)	In mice, no increased incidence of tumours was found at exposures similar to the mean human exposure, but an increased incidence of haemangiosarcoma was observed at higher exposures.	
Use in children	Experience with Pregabalin capsule in patients under 18 years is limited. Therefore, the use of Pregablin capsule in children is not recommended.	
Abuse, misuse and drug dependence	Reports of abuse, misuse and drug dependence have been received from patients. This has not been observed during clinical studies.	However, before taking pregabalin patients should tell their doctor if they have a history of alcoholism or any drug abuse or dependence. The patient should not take more medicine

Missing information

Risk	What is known
Use in pregnancy, lactation	There are no adequate data on the use of pregabalin in pregnant women. Studies in pregabalin in animals have shown toxicity in the animal fetuses at high doses, but the potential risk in humans is not known. Pregabalin should not be taken during pregnancy, unless specifically recommended by a doctor. Effective contraception must be used by women of child-bearing potential. If patients are pregnant or breastfeeding, think they may be pregnant or are planning to have a baby, patients should ask their doctor or pharmacist for advice before taking pregabalin. It is not recommended to breast-feed while using pregabalin as it is not known if pregabalin passes into breast milk. Patients should ask their doctor or pharmacist for advice before taking any medicine while breastfeeding.

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

No post authorisation development plan was proposed.

VI.2.7 Summary of changes to the Risk Management Plan over time

Table 2. Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
01.00	22-MAY-2014	**Identified Risks:** • Hypersensitivity reaction • Dizziness, somnolence, loss of consciousness, mental impairment. • Blurred vision • Renal failure • Withdrawal reaction • Congestive heart failure **Potential Risks:** • Sucidal behaviour • Drug abuse • Encephalopathy • **Missing Information:** • Use in pregnancy, lactation • Use in children	Initial version.
02.00	22.12.2014	**Identified Risks:** • Hypersensitivity and allergic reactions • Dizziness, somnolence, loss of consciousness, syncope and potential for accidential injury • Congestive heart failure • Weight gain • Peripheral oedema and oedema-relevant events • Discontinuation events	

Version	Date	Safety Concerns	Comment
		• Drug interactions (lorazepam, ethanol and CNS depressants) • Euphoria • Vision-related events • Abuse, misuse and drug dependence **Potential Risks:** • Suicidality • Haemangiosarcoma • Off-label use in paediatric patients **Missing information:** • Use in pregnancy, lactation	
03.00	01.07.2015	**Identified Risks:** • Abuse, misuse and drug dependence ➔ Correction in Part II, table 1 Correction of typing mistakes	