VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Epilepsy: It is the commonest neurological condition, characterized by recurrent seizures, affecting people of all ages, race and social class. There are an estimated 50 million people with epilepsy in the world. In general, the incidence of epilepsy in developed countries is taken to be around 50 per 100,000 (range 40−70 per 100,000/year), while the incidence of epilepsy in resource-poor countries is generally higher in the range of 100−190 per 100,000/year. Epilepsy can be divided into two main groups (focal or generalised) depending on the source of the seizure within the brain. When compared partial versus generalised seizures, generalized seizures were more common in the first five years of life, the incidence was similar for both between the ages of 6 and 24, and partial seizures were at least twice as common as generalised onset seizures in adults over 24 years.

Peripheral neuropathic pain: It can be described as situations where nerve roots or peripheral nerve trunks have been injured by mechanical and/or chemical stimuli that exceeded the physical capabilities of the nervous system. Neuropathic pain is often described as burning, stabbing, shooting, aching, or like an electric shock.Various conditions that can cause neuropathic pain include – Trigeminal neuralgia, Postherpetic neuralgia, Diabetic neuropathy, Phantom limb pain following an amputation, Multiple sclerosis, Pain following chemotherapy, HIV infection, Alcoholism, Cancer, Atypical facial pain and Various other uncommon nerve disorders. Diabetic neuropathy is the most common peripheral neuropathy in the western world, including roughly 2/3 of diabetic patients. The incidence of painful diabetic peripheral neuropathy was 15.3/100,000 and estimated prevalence range from 11% to 26% (15%) proportion of patients with diabetes. For post-herpetic neuralgia the estimated incidence in general population was 11–40/100,000 (11/100,000) and 7% to 27% was the prevalence in patient with herpes zoster.

VI.2.2 Summary of treatment benefits

Epilepsy cannot be cured with medication. However, various medicines can prevent seizures. They work by stabilising the electrical activity of the brain. Seizures can be well controlled by medication in about 4 out of 5 cases.

More than half the children with medication-controlled epilepsy can eventually stop medications and live a seizure-free life. Many adults also can discontinue medication after two or more years without seizures.

There are many drugs available for treating epilepsy, called anticonvulsant or anti-epileptic drug (AED). Selection of an anticonvulsant medication depends on an accurate diagnosis of patient’s seizure type and epilepsy syndrome, but finding the right medication and dosage can

be complex. Although some anticonvulsants (e.g. lamotrigine, topiramate, valproic acid, zonisamide) have multiple mechanisms of action, Mechanisms of gabapentin is based on H-current modulators and by blocking the unique binding sites.

If using just one drug doesn't control seizures, one or more drugs may be administrated at the same time, known as combination therapy, or sometimes adjunctive or add-on therapy or polytherapy.

Gabapentin is used to treat partial and secondarily generalized seizures. Gabapentin does not prevent primary generalized seizures. Gabapentin seizures control and pain-control is not well established, but is seem that Gabapentin affects same chemicals and nerves in the body that are involved in the cause of seizures and some types of pain.

Gabapentin is usually used as an additional/adjunctive seizure medicineas it does not interact with other seizure medicines. Rarely gabapentin is also used alone to treat partial seizures.

Besides controlling seizures, gabapentin is also helpful in adults for some kinds of pain that follows "shingles" (called post-herpetic neuralgia) or in patients with diabetes (painful diabetic neuropathy).

VI.2.3 Unknowns relating to treatment benefits

There are no adequate data from the use of gabapentin in pregnant women.

VI.2.4 Summary of safetyconcerns

Important identified risks

Risk	What is known	Preventability

Drug Rash with Eosinophilia (increased number of eosinophils in the blood) and Systemic Symptoms (fever, swollen lymphnodes, inflammation of liver) [DRESS syndrome]	A group of side effects that could include swollen lymph nodes (isolated small raised lumps under the skin), fever, rash, and inflammation of liver occurring together have been reported in patients taking antiepileptic drugs including gabapentin. If such signs are present, the patient should be evaluated immediately.	Gabapentin should be discontinued if it is considered of be the cause of DRESS syndrome, because the reaction is severe and may be fatal.
Concomitant use of gabapentin with opioids	Concomitant use of gabapentin with opioids may cause symptoms like sleepiness and/or decrease in breathing.	If you are taking any medicines containing opioids (such as morphine), please tell your doctor or pharmacist as opioids may increase the effect of gabapentin.
Abuse and dependence	Cases of abuse and dependence have been reported for gabapentin from the post-marketing experience.	Talk to your doctor if you have a history of abuse or dependence.

Important potential risks

Risk	**What is known**

Thoughts or attemptsof harming or killing oneself [Suicide ideation andbehaviour]	Gabapentin could cause a small increased risk of suicidal thoughts (thoughts of harming or killing themselves) or suicidal attempts in people who take this drug. The mechanism of this risk is unknown. The patients may experience: talking or thinking about wanting to hurt themselves or end their life, becoming preoccupied with death and dying, becoming depressed or having the depression get worse, withdrawing from friends and family. Patient's family members and caregivers should pay close attention to any unusual day-to-day changes in mood, behavior and actions. These changes can happen quickly so it is important to be mindful of any sudden differences. If they notice any of these signs, they should contact the doctor immediately.
Inflamed pancreas [Pancreatitis]	Pancreatitis (inflamed pancreas) may occur under treatment with Gabapentin. The patients may experience severe upper abdominal pain which may radiates to the back, nausea, vomiting. These may be symptoms of acute pancreatitis. The patient should contact the doctor immediately. If a patient develops acute pancreatitis under treatment with gabapentin, discontinuation of gabapentin should be taken into account.

Fits [Seizure]	Gabapentin is used to treat seizures (epileptic fits) that begin in a limited area of the brain. These are called partial seizures. Some of them spread throughout the rest of the brain. They are called secondarily generalized seizures. Gabapentin does not prevent seizures that begin on both sides of the brain at the same time, called primary generalized seizures. Brain cells need to work (fire) at a certain rate to function normally. During a seizure, brain cells are forced to work much more rapidly than normal. Gabapentin helps prevent brain cells from working as fast as a seizure requires them to. In this way, seizures can be stopped when they are just beginning. There is not completely understood how gabapentin works in the brain to stop seizures. It probably causes brain cells to make more of a chemical (called GABA) that stops brain cells from firing. The patient should not stop taking an epilepsy medication (including gabapentin) abruptly, because this may possibly lead to seizures. Gabapentin sometimes worsens absence seizures (absence seizures are brief episodes of staring, brief loss of awareness). People who have seizures of these types should not use it.

Missing information

Risk	**What is known**

Use during pregnancy and lactation	Gabapentin should not be taken during pregnancy, unless the doctor advises otherwise. Effective contraception must be used by women of child-bearing potential. There have been no studies specifically looking at the use of gabapentin in pregnant women, but other medications used to treat seizures have reported an increased risk of harm to the developing baby, particularly when more than one seizure medication is taken at the same time. Therefore, whenever possible, the patient should try to take only one seizure medication during pregnancy and only under the advice of the doctor. The patient should not suddenly discontinue taking this medicine as this may lead to a breakthrough seizure, which could have serious consequences for the mother and for her baby. Gabapentin passes in human milk. Because the effect on the baby is unknown, it is not recommended to breast-feed while using Gabapentin.
Effects of long-term use in children and adolescents	The effects of long-term (greater than 36 weeks) gabapentin therapy on learning, intelligence, and development in children and adolescents have not been adequately studied. The benefits of prolonged therapy must therefore be weighed against the potential risks of such therapy.

VI.2.5 Summary of additional 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 studies planned.

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

Version	Date	Safety Concern	Comments
2.0	03 February 2016	Below Important identified risks have been included in the RMP: • Concomitant use with opioids • Abuse and dependence Below safety concern has been changed as important identified risk from important potential risk in the RMP: • Drug Rash with • Eosinophilia and Systemic • Symptoms (DRESS)	The safety concerns and relevant sections have been changed based on Day 70 RMP assessment report (UK/H/6170/01-03/DC) of gabapentin. This RMP has been updated as Day 70 and Day 100 assessment reports.