VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Epilepsy

Epilepsy is a central nervous system (neurological disorder) in which nerve cell activity in the brain becomes disrupted, causing seizures (fits) or periods of unusual behaviour, sensations and sometimes loss of consciousness.

Epilepsy affects about 22 million people as of 2013. It affects 1% of the population by age 20 and 3% of the population by age 75. It is more common in males than females with the overall difference being small. Most of those with the disorder (80%) are in the developing world.

The estimated commonness of active epilepsy (as of 2012) is in the range 3–10 per 1,000, with active epilepsy defined as someone with epilepsy who has had a least one unprovoked seizure in the last five years. Epilepsy begins each year in 40–70 per 100,000 in developed countries and 80–140 per 100,000 in developing countries.

VI.2.2 Summary of treatment benefits

Levetiracetam has positive effects in reducing seizures (fits) in patients with epilepsy, both in addition to another therapy and as a therapy taken alone.

Levetiracetam has many therapeutic benefits for patients with epilepsy. It has favorable characteristics in the way that the human body absorbs, distributes, and gets rid of the drug and a low possibility for causing drug-drug interactions. Starting dosages suggested by healthcare professionals have positive effects; therefore, patients can have some protection from seizures soon after they start taking levetiracetam.

The most common adverse effects observed with levetiracetam are mild and include sleepiness, feeling of weakness, and dizziness. Studies have shown that levetiracetam is well tolerated, with effectiveness comparable or slightly better than that observed with other new antiepileptic drugs. Levetiracetam may be particularly useful in patients who do not respond to other antiepileptic drugs, patients receiving drugs with high possibility of causing drug-drug interactions, or those having liver problems.

VI.2.3 Unknowns relating to treatment benefits

Safety and effectiveness of levetiracetam treatment as a therapy taken alone in patients below the age of 16 have not been studied.

Limited data are available regarding levetiracetam use during pregnancy (including worsening of seizure management during pregnancy).

Lifelong effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children and reduced bone mineral density (a measure indicating the amount of mineral in bones) after prolonged levetiracetam exposure remain unknown.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Abnormal behaviour	Abnormal behaviour is an uncommon side-effect of levetiracetam (may affect up to 1 in 100 people).	Patients (and caregivers of patients) should be advised to seek medical advice if signs of abnormal behaviour appear.
Thoughts and actions to cause one's own death [Suicidality (in patients aged 4 years and older)]	Thoughts and actions to cause one's own death (suicide, suicide attempt, suicidal ideation and behaviour) have been reported in patients treated with levetiracetam. Suicide attempt and suicidal ideation is an uncommon side-effect of levetiracetam (may affect up to 1 in 100 people). Suicide is a rare side-effect of levetiracetam (may affect up to 1 in 1,000 people). Clinical trials of anti-epileptic medicinal products have shown a small increased risk of suicidal thoughts and behaviour in patients. The mechanism of this risk is not known.	Patients should be monitored for signs of depression and/or suicidal ideation and behavior and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice if signs of depression and/or suicidal ideation or behavior appear. If suicidal ideation or behaviour is seen in the patient, then levetiracetam should be stopped immediately. The treating doctor should check the patient and initiate another therapy.
Hematologic abnormalities (Blood dyscrasias)	Levetiracetam can cause blood abnormalities. Blood abnormalities occurred in clinical trials and included decreases in red blood cell (RBC) counts, hemoglobin, and hematocrit (amount of red blood cells in the blood), and increases in eosinophil counts. Decreased white blood cell (WBC) and neutrophil counts also occurred in clinical trials. Cases of agranulocytosis (severe reduction in number of white	If patients get any of these side effects, they must talk to their doctor or pharmacist.

	blood cells which makes infections more likely) have been reported in the postmarketing setting. Decreased number of blood platelets (thrombocytopenia) and decreased number of white blood cells (leukopenia) are uncommon side-effects of levetiracetam (may affect up to 1 in 100 people). Decreased number of all blood cell types (pancytopenia) is a rare side-effect of levetiracetam (may affect up to 1 in 1,000 people).	
Low blood levels of sodium (Hyponatremia)	Low blood levels of sodium (hyponatremia) can cause tiredness and confusion, muscle twitching, fits and coma. Hyponatraemia is a rare adverse reaction of levetiracetam (may affect up to 1 in 1,000 people).	If patients get any of these side effects, they must talk to their doctor or pharmacist.
Decreased levetiracetam efficacy with concomitant use of osmotic laxative macrogol	There have been isolated reports of decreased levetiracetam effectiveness when the osmotic laxative macrogol has been taken together with oral levetiracetam.	Macrogol should not be taken orally for one hour before and for one hour after taking levetiracetam.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Seizure worsening	There is evidence that levetiracetam use might be associated with the risk of seizure worsening, as have been reported in different studies.

Missing information

Risk	What is known
Long term effects on learning, growth, intelligence, endocrine function, puberty and	Available data in children did not show impact on growth and puberty. However, lifelong effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children remain unknown.

Risk	What is known
childbearing potential in children	
Use during pregnancy (including worsening of seizure management during pregnancy)	Postmarketing data from several prospective pregnancy registries have shown outcomes in over 1,000 women exposed to levetiracetam as a therapy taken alone (monotherapy) during the first trimester of pregnancy. Overall, these data do not suggest a significant increase in the risk for major birth defects, although a teratogenic risk cannot be completely excluded. Therapy with many antiepileptic medicinal products is associated with a higher risk of birth defects than monotherapy and, therefore, monotherapy should be considered. Studies in animals have shown reproductive toxicity. Levetiracetam is not recommended during pregnancy and in women of childbearing potential not using contraception unless clinically necessary. Physiological changes during pregnancy may change levetiracetam concentration. Decrease in levetiracetam plasma concentrations has been observed during pregnancy. This decrease is more notable during the third trimester. Pregnant women treated with levetiracetam must be appropriately clinically protected. Stopping antiepileptic treatments may cause worsening of the disease which could cause harm to the mother and the foetus.
Decreased bone mineral density after prolonged exposure	There is evidence that prolonged exposure to levetiracetam use might result to decreased bone mineral density (a measure indicating the amount of mineral in bones), as have been reported in different studies.

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