VI.2 Elements for a Public Summary

(a) VI.2.1 Overview of disease epidemiology

Lacosamid Stada is a medicine used for as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16-18 years) patients with epilepsy.

Epilepsy is defined by the recurrence of spontaneous/unprovoked seizures constitutes a vast ensemble of very diverse clinical situations which differ by age of onset, type of seizures, aetiological background, resulting handicap, prognosis and response to treatment. More than 50 million adults and children are estimated to suffer from epilepsy world-wide. The two highest peaks of incidence are in children and in the elderly population (above 65 years). Prevalence estimates of epilepsy in the total population varies from 4 to 8 per 10000 subjects.

The classification of epileptic seizures is based on clinical manifestation. The 3 main types are generalized, partial-onset (which may become secondarily generalized), and unclassified. Partial-onset epilepsies, associated with a local cerebral lesion, are the most frequent, representing approximately 60% of cases. Generalized epilepsies represent approximately 30% of cases. In the remaining 10% of seizures, the classification is uncertain.

(b) VI.2.2 Summary of treatment benefits

Lacosamid Stada is a generic medicine which means that it is similar to a reference medicine already authorised in the European Union (EU). Lacosamid Stada studies in people have been limited to a study to determine that it is bioequivalent to the reference medicine. Hence, its benefits and risks are taken as being the same as the reference medicine's.

The CHMP decided that the benefits of the originator product Vimpat are greater than its risks. Vimpat was more effective than placebo (a dummy treatment) at reducing seizures in three main studies involving a total of 1,308 patients also taking other epilepsy medicines. Patients added Vimpat taken by mouth at a dose of 200 mg, 400 mg or 600 mg a day, or placebo to their existing treatment of up to three other epilepsy medicines. The main measure of effectiveness was the number of patients whose number of seizures was at least halved after 12 weeks of treatment with a stable dose. Taking the results of the three main studies together, 34% of the patients taking Vimpat 200 mg a day and 40% of the patients taking Vimpat 400 mg a day with their existing treatment had a reduction in their seizures by at least half. This compared with 23% of the patients taking placebo. The 600-mg dose was as effective as the 400-mg dose, but it had more side effects.

A fourth study involving 888 recently diagnosed patients showed that Vimpat, used on its own by mouth at a dose of 200 mg to 600 mg a day, was at least as effective as carbamazepine, another medicine for epilepsy. The main measure of effectiveness was the proportion of patients who did not have a seizure for at least 6 months after reaching a stable dose. This was found to be 90% in those taking Vimpat and 91% in those taking carbamazepine. Around 78% of Vimpat-treated and 83% of carbamazepine-treated patients did not have a seizure for 12 months.

Two additional studies looked at the appropriate duration of the infusion for Vimpat solution and compared its safety with that of placebo infusions in a total of 199 patients. An additional study in 118 patients was carried out to test that loading doses of 200 mg Vimpat by infusion, followed by

maintenance doses taken by mouth, can be applied safely and that adequate levels in the body are achieved.

(c) VI.2.3 Unknowns relating to treatment benefits

(d) There are no adequate data from the use of lacosamide in pregnant women. Studies in animals did not indicate any teratogenic effects in rats or rabbits, but embryotoxicity was observed in rats and rabbits at maternal toxic doses. The potential risk for humans is unknown.

(e) It is unknown whether lacosamide is excreted in human breast milk. Animal studies have shown excretion of lacosamide in breast milk. For precautionary measures, breast-feeding should be discontinued during treatment with Lacosamid Stada.

(f) The safety and efficacy of lacosamide in children aged below 16 years have not yet been established. No data are available.

(g) VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Cardiac AEs that may be potentially associated with PR interval prolongation and sodium channel modulation	Prolongations in PR interval with lacosamide have been observed in clinical studies.	Lacosamid Stada should be used with caution in patients with known conduction problems or severe cardiac disease such as a history of myocardial infarction or heart failure. Caution should especially be exerted when treating elderly patients as they may be at an increased risk of cardiac disorders or when Lacosamid Stada is used in combination with products known to be associated with PR prolongation.
Suicidality	Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications.	Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge
Dizziness	Treatment with lacosamide has been associated with dizziness	Patients should be advised to exercise caution until they are

	which could increase the occurrence of accidental injury or falls.	familiar with the potential effects of the medicine

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Hepatotoxicity	Abnormalities in liver function tests have been observed in controlled trials with lacosamide in adult patients with partial-onset seizures who were taking 1 to 3 concomitant anti-epileptic drugs. Elevations of ALT to ≥3x ULN occurred in 0.7% (7/935) of lacosamide patients and 0% (0/356) of placebo patients.
Potential for worsening of seizures	Patients treated with the medicinal product may be at an increased risk of developing this safety concern.
Potential for abuse as an CNS-active product	There is a risk for abuse of Lacosamid Stada as an CNS-active product.
Potential for off-label use of a loading dose in acute conditions such a status epilepticus	Administration of a loading dose has not been studied in acute conditions such as status epilepticus.

Missing information

Risk	What is known
Use in pregnant and lactating women	There are no adequate data from the use of lacosamide in pregnant women. The potential risk for humans is unknown. Lacosamid Stada should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus). If women decide to become pregnant, the use of this product should be carefully re-evaluated. It is unknown whether lacosamide is excreted in human breast milk. Animal studies have shown excretion of lacosamide in breast milk. For precautionary measures, breast-feeding should be discontinued during treatment with Lacosamid Stada.
Use in paediatric patients	The safety and efficacy of lacosamide in children aged below 16 years have not yet been established. No data are available.

(h) 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 healthcare 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.

The Summary of Product Characteristics and the Package leaflet for Lacosamid Stada can be found in the Lacosamid Stada's EPAR page

This medicine has no additional risk minimisation measures

(i) VI.2.6 Planned post authorisation development plan

Not applicable

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

Not applicable