SUMMARY OF THE RISK MANAGEMENT PLAN

FOR

BRIVIACT® (BRIVARACETAM)

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SUMMARY OF THE RISK MANAGEMENT PLAN

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine.

The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary for brivaracetam is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, eg, by mentioning risks occurring in populations or indications not included in the Swiss marketing authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Briviact in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorised by Swissmedic. UCB-Pharma SA is fully responsible for the accuracy and correctness of the content of this published RMP summary for Briviact.

OVERVIEW OF DISEASE EPIDEMIOLOGY

Briviact is an epilepsy medicine that is used as 'add-on' therapy to treat partial-onset seizures (epileptic fits starting in one specific part of the brain) in adults and adolescents from the age of 16 years.

Epilepsy is a long-term condition of the brain and is characterised by recurring seizures (fits). It is one of the most common diseases affecting the brain – about 70 million people worldwide have epilepsy. Epilepsy is most common among young children and older adults. In children, epilepsy may be inherited or it can be caused by problems during pregnancy or birth. In both children and adults, epilepsy can be caused by head injury, infection, brain tumours, or stroke.

SUMMARY OF TREATMENT BENEFITS

Briviact contains the active substance brivaracetam and it was found more effective than placebo (a dummy treatment) at reducing seizures. This was shown in three main studies involving a total of 1,558 patients aged 16 years and above. Either Briviact or placebo was added to patients' usual epilepsy treatment. Taking the studies together, the frequency of seizures was at least halved in 34 to 38% of those adding Briviact at doses from 25 to 100 mg twice a day. This compares with 20% in those adding placebo.

UNKNOWNS RELATING TO TREATMENT BENEFITS

There is not enough information available on the use of Briviact in the following patient groups:

- Children aged under 16 years
- Adults aged above 65 years

SUMMARY OF SAFETY CONCERNS

Important identified risks

Suicidality and aggression are important side effects that are likely to be caused by brivaracetam in small numbers of patients. What is known and how these side effects can be prevented are described in Table 1.

Table 1: Summary of important identified risks

Risk	What is known	Preventability
Thoughts about suicide and behaviour relating to suicide (suicidality)	Suicide-related events have been reported more often in people who have epilepsy than in the general population. Common additional disorders in patients with epilepsy that increase the risk of suicide include depression and learning difficulties or disability. A small increased risk of suicide-related events has also been reported in patients with epilepsy taking antiepileptic drugs including Briviact.	Patients should be advised to immediately report to their doctor and to seek medical advice for suicidal thoughts, behaviours, or changes in mood. Healthcare providers, caregivers, and family members must watch the patient closely for any signs of suicidal thoughts, behaviours, or changes in mood to help prevent suicide attempts.
Feeling of anger or hostility towards others or self (aggression)	A small increased risk of aggression has been reported in patients with epilepsy taking antiepileptic drugs including Briviact.	Patients experiencing aggression should be advised to immediately report this to their doctor and to seek medical advice. Healthcare providers, caregivers, and family members must watch the patient closely for signs of aggression to prevent potential harm.

Important potential risks

Important side effects that may be caused by brivaracetam are described in Table 2.

Table 2: Summary of important potential risks

Risk	What is known
Low blood levels of neutrophils (a type of white blood cells (neutropenia)	There have been reports of a reduction in neutrophils in patients taking Briviact during clinical studies. A slight decrease in neutrophils is not usually serious, but a large decrease can be serious and increase the chance of infection.
Worsening of seizures	Seizures may increase or become worse while taking Briviact. However, these could be the results of changes in the patient's overall health or the underlying epilepsy getting worse.

Table 2: Summary of important potential risks

Risk	What is known
Intentionally and frequently exceeding the prescribed dose of the medicine (abuse potential)	Briviact may produce a calming effect or sleepiness, especially when taken at higher doses. Briviact should be used only for the treatment of seizures. Abuse of brivaracetam (the active substance in Briviact) may cause serious medical problems, particularly problems that affect the nervous system – for example sleepiness, abnormal gait (way of walking), and confusion.
Taking the medicine in a way that is not described in the product information (off-label use)	There is a risk that Briviact might be used for types of epilepsy for which it is not licensed or in children. Use of Briviact outside of its intended use may result in a lack of effect and uncontrolled disease.

Missing information

The groups of patients where side effects from brivaracetam are not fully known are described in Table 3.

Table 3: Summary of missing information

Risk	What is known
Use during pregnancy and breastfeeding	There is limited information on the safety of Briviact in women who are pregnant or breastfeeding and on their babies. In clinical studies, 36 pregnancies were reported in patients taking Briviact, and the women stopped taking Briviact as soon as they became aware of their pregnancy (usually within first 12 weeks). There appeared to be no increase in the rate of pregnancy loss in these women, and there were no reports of abnormalities in babies. Briviact should not be used during pregnancy unless clinically necessary. A decision should be made whether to discontinue breastfeeding or to discontinue Briviact, taking into account the benefit of the medicine to the mother.
Use in patients with liver damage (hepatic impairment)	So far in the clinical studies on Briviact, no one has developed liver disease. However, these studies did not include patients who already had liver damage, so the long-term effect of Briviact in such patients is not known. When a single dose of Briviact was given to patients with liver damage, the levels of brivaracetam in the blood were increased. Because of this effect, patients with liver disease should take a smaller dose of Briviact.
Use in patients whose kidneys no longer work well enough for the body's needs (end-stage renal disease) who are on dialysis	Brivaracetam is removed from the body by the kidneys. A study that included patients with epilepsy and kidney disease showed that Briviactcan still be used in these patients without a dose reduction. However, this study did not include patients with end-stage kidney damage and who were on dialysis. Therefore, Briviact is not recommended in these patients.

Table 3: Summary of missing information

Risk	What is known
Use in adults aged above 65 years	Forty-four patients aged above 65 years took part in clinical studies on Briviact for epilepsy. Although the pattern of side effects seemed similar to that in younger adults, there is not enough information on the safety of Briviact in adults above 65 years to be sure that there are no adverse effects specific for such patients.
Overdose	Few patients took an overdose of Briviact during the clinical studies. Although the most frequent side effects after taking a very high dose are likely to be sleepiness and dizziness, there is not enough information on the safety of Briviact after an overdose to be sure that there are not more serious side effects.
Long-term safety	Although some of the studies for Briviact have run for over 8 years, it is still possible that some rare effects may not have been picked up.

SUMMARY OF RISK MINIMIZATION MEASURES BY SAFETY CONCERN

All medicines have a product information which provides physicians, pharmacists, and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as ‘routine risk minimization measures’.

The product information and the package leaflet for Briviact can be found on the Swissmedic website (www.swissmedicinfo.ch).

PLANNED POSTAUTHORIZATION DEVELOPMENT PLAN

List of studies in postauthorization development plan

Study/activity (including study number)	**Objectives**	**Safety concerns/efficacy issue addressed**	**Status**	**Planned date for submission of (interim and) final results**
Participation in and sponsorship of antiepileptic drug Pregnancy Registries including: European and International Registry of Antiepileptic Drugs in Pregnancy and North American Antiepileptic Drug Pregnancy Registry	Collect data on pregnancy	Pregnancy and lactation	Ongoing	Ongoing – will be discussed in Periodic Safety Update Reports

Studies that are a condition of the marketing authorization

None.