

## Summary of the risk management plan (RMP) for Briviact (brivaracetam)

This is a summary of the risk management plan (RMP) for Briviact, which details the measures to be taken in order to ensure that Briviact is used as safely as possible. For more information on RMP summaries, see [here](#).

This RMP summary should be read in conjunction with the EPAR summary and the product information for Briviact, which can be found on Briviact's [EPAR page](#).

### 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 is 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 on the use of Briviact in the following groups:

- children aged under 16 years
- adults aged above 65 years

## Summary of safety concerns

### *Important identified risks*

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Thoughts about suicide and behaviour relating to suicide (suicidality)	Suicide-related events have been reported more often in people with 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 epilepsy medicines including Briviact.	Patients should be advised to immediately report to their doctor and to seek medical advice for suicidal thoughts, behaviour, or changes in mood.  Healthcare providers, caregivers, and family members must watch the patient closely for any signs of suicidal thoughts, behaviour, 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 epilepsy medicines 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*

<b>Risk</b>	<b>What is known</b>
Low blood levels of neutrophils (a type of white blood cell) (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 result of changes in the patient's overall health or the underlying epilepsy getting worse.
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 its intended use may result in a lack of effect and uncontrolled disease.

### Missing information

<b>Risk</b>	<b>What is known</b>
Use during pregnancy and breastfeeding	<p>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.</p> <p>A decision should be made whether to discontinue breastfeeding or to discontinue Briviact, taking into account the benefit of the medicine to the mother.</p>
Use in patients with liver damage (hepatic impairment)	<p>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.</p> <p>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.</p>
Use in patients whose kidneys no longer work well enough for the body's needs (end-stage renal disease) who are on dialysis	<p>Brivaracetam is removed from the body by the kidneys. A study that included patients with epilepsy and kidney disease showed that Briviact can still be used in these patients without a dose reduction. However, this study did not include patients with end-stage kidney damage who were on dialysis. Therefore, Briviact is not recommended in these patients.</p>
Use in adults aged above 65 years	<p>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.</p>
Overdose	<p>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.</p>
Long-term safety	<p>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.</p>

### Summary of 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, 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 minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Briviact can be found on Briviact's [EPAR page](#).

## Planned post-authorisation development plan

### *List of studies in post-authorisation development plan*

<b>Study/activity (including study number)</b>	<b>Objectives</b>	<b>Safety concerns /efficacy issue addressed</b>	<b>Status</b>	<b>Planned date for submission of (interim and) final results</b>
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	Planned start once Briviact is authorised and information becomes available	Ongoing – will be discussed in Periodic Safety Update Reports

### *Studies which are a condition of the marketing authorisation*

None

This summary was last updated in December 2015.