North Central London
Joint Formulary Committee

Factsheet

BRIVARACETAM (Briviact®)

Second-line add on option for generalised epilepsy, myoclonic epilepsy and focal epilepsy

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Document Control		
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November 2023	V1	Factsheet produced by UCLH specialist pharmacists and NCL ICB Barnet borough Medicines Management Team Agreed by NCL Shared Care Group: 14th November 2023

Disclaimer
Factsheets support GPs in taking ongoing responsibility for continuing a medicine initiated in secondary care. It differs from a shared care agreement where secondary cares retain a proportion of responsibility for ongoing care.

This document is intended for use by healthcare professionals to aid the treatment of patients within NCL. It should not be used for marketing purposes. If you identify information within this document that is inaccurate, please report to admin.ncl-mon@nhs.net.

Indication information

As per local formulary agreement, brivaracetam is initiated by a Consultant Neurologist and is continued by the patients GP. It may be prescribed as a second line adjunctive treatment in children, young people and adults from the age of 2 years for generalised epilepsy, myoclonic epilepsy, and focal epilepsy, in line with NICE guidance, for use in patients who could not tolerate levetiracetam or, exceptionally, in patients eligible for levetiracetam but deemed by the specialist epilepsy team to be at high risk of behavioural side effects.

The hospital team will:

1. Provide the patient with initial information regarding the treatment and possible adverse effects.
2. Initiate and optimise (stabilise) treatment and inform GP via letter when patient is stable on dose so that GP can continue prescribing (timescale will be dependent on individual dose titration but typically after 3 months).
3. Provide advice and guidance regarding dose adjustment depending on tolerability.
4. Clinically supervise patient by routine ongoing clinic follow-ups on average every 6 months and monitor response to treatment.

Checklist for GPs:

1. Monitor patient's overall health and wellbeing.
2. Monitor for signs for decreased efficacy of brivaracetam (i.e. increase in seizure activity), adverse effects and possible medicines interaction.
3. Report any problems (e.g. adverse effects, non-compliance reported by the patient) to the Hospital Epilepsy team.
4. Prescribe titration doses, maintenance dose and adjust dose on recommendation of consultant and inform the patient of any dose changes.

Dose and Administration

The maximum licensed dose is 200mg/day

The dose should be taken in two equally divided doses, approximately 12 hours apart.

Table 1: Dosing schedule of brivaracetam in adults and children for initiation and maintenance

Recommended starting dose	Recommended maintenance dose	Therapeutic dose range*
Adolescents and children weighing 50 kg or more, and adults		
50 mg/day (or 100 mg/day)**	100 mg/day	50 - 200 mg/day
Adolescents and children weighing from 20 kg to less than 50 kg		
1 mg/kg/day (up to 2 mg/kg/day)**	2 mg/kg/day	1 – 4 mg/kg/day

Children weighing from 10 kg to less than 20 kg		
1 mg/kg/day (up to 2.5 mg/kg/day)**	2.5 mg/kg/day	1 – 5 mg/kg/day

* Based on individual patient response, the dose may be adjusted within this effective dose range.

** Based on consultant's assessment of need for seizure control

Elderly (65 years of age and above): No dose adjustment is needed in elderly patients.

Renal impairment*:*
Adults: No dose adjustment is needed in patients with impaired renal function. Brivaracetam is not recommended in end-stage renal disease patients undergoing dialysis due to lack of data.

Paediatrics: Based on data in adults, no dose adjustment is necessary in paediatric patients with impaired renal function. No clinical data are available in paediatric patients with renal impairment.

Hepatic impairment*:*
Adults: Exposure to brivaracetam was increased in adult patients with chronic liver disease.
In patients with hepatic impairment, the following adjusted doses, administered in 2 divided doses, approximately 12 hours apart, are recommended for all stages of hepatic impairment (see table below for recommended dosing).

Paediatrics: No clinical data are available in paediatric patients with hepatic impairment. The Specialist will advise on any dose adjustments required.

Table 2: Starting dose schedule for adolescents and children with maximum daily dose

Age and body weight	Recommended starting dose	Recommended maximum daily dose
Adolescents and children weighing 50 kg or more, and adults	50 mg/day	150 mg/day
Adolescents and children weighing from 20 kg to less than 50 kg	1 mg/kg/day	3 mg/kg/day
Children weighing from 10 kg to less than 20 kg	1 mg/kg/day	4 mg/kg/day

Method of administration: Brivaracetam film-coated tablets must be taken orally and swallowed in whole with liquid and may be taken with or without food.

Patients not being able to swallow tablets whole or patients for whom the dose cannot be met with the use of whole tablets should use brivaracetam 50 mg/5ml oral solution.

Brivaracetam oral solution can be diluted in water or juice shortly before swallowing and may be taken with or without food.

Missed doses: If one or more doses are missed, it is recommended that the patient take a single dose as soon as they remember and take the next scheduled dose at the usual morning or evening time.

Discontinuing treatment: Avoid abrupt withdrawal. Weaning regimens will be determined by the specialist team and continued in community by GPs following specialist advice detailed in a letter.

Adverse Effects

Adverse effect	Frequency	Suggested management by GP
Dizziness, somnolence	Very common	If these effects remain unresolved, refer back to specialist team
Fatigue	Common	If these effects remain unresolved, refer back to specialist team
Influenza, upper respiratory tract infection, cough	Common	If these effects remain unresolved, refer back to specialist team
Decreased appetite	Common	If these effects remain unresolved, refer back to specialist team
Depression, anxiety	Common	If these effects remain unresolved, refer back to specialist team
Insomnia, irritability, vertigo	Common	If these effects remain unresolved, refer back to specialist team
Nausea, vomiting, constipation	Common	If these effects remain unresolved, refer back to specialist team
Convulsions	Common	Refer back to specialist team if reported
Suicidal ideation, psychotic disorder, aggression	Uncommon	Refer back to specialist team if reported
Neutropenia	Uncommon	Refer back to specialist team if reported
Type I hypersensitivity	Uncommon	Refer back to specialist team if reported

The frequencies are defined as follows: very common (≥ 1/10), Common (≥1/100 to <1/10), Uncommon (≥ 1/1,000 to < 1/100).

Healthcare professionals are asked to report any suspected adverse reactions using the Yellow Card Scheme.

Contraindications

Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the excipients.

Special Warnings and Precautions for Use

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic drugs (AEDs), including brivaracetam, in several indications. A meta-analysis of randomized placebo-controlled clinical studies of AEDs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known, and the available data do not exclude the possibility of an increased risk for brivaracetam.

Patients should be monitored for signs of suicidal ideation and behaviours (i.e. emergence or worsening of depression, unusual changes in mood/behaviour, or suicidal thoughts, or self-harm) during routine reviews, and patients should be informed how and to whom they should report them to; a referral back to the initiating specialist should be made to determine appropriate treatment. Patients (and caregivers of patients) should be advised to seek medical advice should any signs of suicidal ideation or behaviour emerge.

Excipients

Tablets: Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take brivaracetam tablets as they contain lactose.

Oral solution: Patients with hereditary fructose intolerance should not take this medicinal product as it contains sorbitol. The oral solution contains methyl parahydroxybenzoate, which may cause allergic reactions (possibly delayed). The oral solution contains propylene glycol which may cause intolerance.

Women of childbearing potential

The consultant should discuss family planning and contraception with women of childbearing potential prior to initiating brivaracetam (see Pregnancy).

If a woman decides to become pregnant, the use of brivaracetam should be carefully re-evaluated; GPs should refer the patient to the specialist team to discuss.

Pregnancy and breast feeding

There is a limited amount of data from the use of brivaracetam in pregnant women. Manufacturer advises avoid unless potential benefit outweighs risk. If a patient becomes pregnant whilst on treatment, please refer back to the specialist team for review.

Brivaracetam is excreted in human breast milk. Studies in rats have shown excretion of brivaracetam in breast milk. A decision should be made whether to discontinue breastfeeding or to discontinue brivaracetam, taking into account the benefit of the medicinal product to the mother. This decision should be made by the obstetrics/epilepsy teams with the patient upon delivery of the baby.

Effects on ability to drive and operate machinery

Patients should be cautioned on the effects on driving and performance of skilled tasks – increased risk of dizziness, somnolence and other central nervous system-related symptoms. Patients should be advised not to drive a car or to operate other potentially hazardous machines until they are familiar with the effects of brivaracetam on their ability to perform such activities.

Drug Interactions

Consumption of alcohol with brivaracetam is not recommended, and the patient should be advised to avoid alcohol prior to initiation.

Brivaracetam plasma concentrations may increase when co-administered with strong CYP2C19 inhibitors (e.g. fluconazole, fluvoxamine) however this has low clinical relevancy.

Brivaracetam plasma concentrations are decreased when co-administered with strong enzyme-inducing AEDs (i.e. carbamazepine, phenobarbital, phenytoin). No dose adjustment is required.

Strong enzyme inducers such as rifampicin or St John's wort (Hypericum perforatum) may reduce systemic exposure to brivaracetam. Monitor for signs of a decrease in brivaracetam efficacy. Consider discussion with specialist on whether any dose adjustments are necessary.

Please refer to SPC/BNF for full information on interactions with brivaracetam and how to manage these interactions.

Clinical Monitoring

No specific blood monitoring of patients is required.
Patients should be monitored for their response to therapy (i.e., whether seizure frequency/severity are affected), and any associated adverse effects (including suicidal ideation).

Contact Details for specialist advice

National Hospital for Neurology and Neurosurgery (NHNN)	
NHNN Hospital Switchboard	020 3456 7890
NHNN Pharmacy Office	020 3448 3327
Epilepsy departmental contact details below	
Epilepsy Specialist Nurses	*uclh.epilepsy@nhs.net* *020 34488627*

References

1. Summary of Product Characteristics for Briviact ® tablets UCB Pharma Limited last updated on eMC on the 01-Jun-2022 accessed via https://www.medicines.org.uk/emc/medicine/31452/ on 17/11/2022
2. Summary of Product Characteristics for Briviact ® oral solution UCB Pharma Limited last updated on eMC on the 01-Jun-2022 accessed via https://www.medicines.org.uk/emc/product/1964/smpc/ on 17/11/2022
3. British National Formulary. Edition 84. Last accessed via https://www.medicinescomplete.com/ on 17/11/2022