Effective Shared Care Agreement (ESCA)

Brivaracetam▼ Oral formulations

ESCA: For adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with severe refractory epilepsy warranting tertiary specialist input for patients who have tried three or more AEDs. The patient has used levetiracetam and has documentation of intolerance and patient is using a third line agent (perampanel, zonisamide, lacosamide, eslicarbazepine) which would be replaced by brivaracetam.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of brivaracetam (oral) in the treatment of severe refractory epilepsy warranting specialist input for patients who have tried three or more AEDs can be shared between the tertiary specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with severe refractory epilepsy are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Tertiary Specialist responsibilities
1. Confirm the diagnosis of severe refractory epilepsy warranting tertiary specialist input for patient who has tried three or more AEDs (please complete appendix 1)
2. Confirm the patient has used levetiracetam (at maximum tolerated dose), responded to treatment but has documentation of intolerance and patient is already using a third line agent (perampanel, zonisamide, lacosamide, eslicarbazepine), which brivaracetam would replace.
3. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient
4. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made
5. Do baseline monitoring prior to initiation of brivaracetam.
6. Initiate treatment and stabilise dose of brivaracetam.
7. Review the patient's condition and monitor response to treatment regularly
8. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay
9. Black triangle▼ drug. Report any suspected adverse events to the MHRA via Yellow Card Scheme https://yellowcard.mhra.gov.uk
10. Ensure clear backup arrangements exist for GPs, for advice and support (**please complete contact details in appendix 1**)

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days						
2. Ensure that the patient has used levetiracetam (at maximum tolerated dose) but has documentation of intolerance and that that the patient is already using a third line agent (perampanel, zonisamide, lacosamide, eslicarbazepine) which is being replaced with brivaracetam.						
3. Prescribe brivaracetam at the dose recommended.						
4. Adjust the dose as advised by the specialist.						
5. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
6. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist						
7. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment.						
8. Refer back to specialist if condition deteriorates.						
9. Black triangle▼ drug. Report any suspected adverse events to the MHRA via Yellow Card Scheme https://yellowcard.mhra.gov.uk						
10. Stop treatment on advice of specialist.						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment
2. Attend regularly for required blood tests and annual health checks.
3. Share any concerns in relation to treatment with brivaracetam with the specialist, clinical nurse specialist or GP.
4. Report any adverse effects to the specialist or GP whilst taking brivaracetam.
5. Attend regular outpatient appointments with the specialist.

SUPPORTING INFORMATION

APC approved indication and rationale	For adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with severe refractory epilepsy warranting tertiary specialist input for patients who have tried three or more AEDs. The patient has used levetiracetam and has documentation of intolerance and patient is using a third line agent (perampanel, zonisamide, lacosamide, eslicarbazepine) which would be replaced by brivaracetam. (please complete appendix 1). <u>Decision making process for choosing 3rd line AED</u>: • In a patient with obvious mood disturbances issues or behavioural issues, the specialist would avoid perampanel. • If a patient has had a problem with a slow sodium channel blocker previously, the specialist cannot use eslicarbazepine. This leaves lacosamide or brivaracetam. • Lacosamide also acts on sodium channels and although some patients tolerate it better than carbamazepine/ eslicarbazepine, it can still cause problems. • If brivaracetam is not available on the formulary, the clinician would have to add in clobazam -long term benzodiazepine dependency and tolerance are recognised side effects. • If patients have clear neuropsychiatric issues, levetiracetam would not be used. Perampanel and zonisamide would potentially be avoided in these patients.	
Licensed indication	Indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy.	
Additional evidence	Despite the large number of antiepileptic drugs (AEDs) available to treat partial-onset seizures (POS), a substantial number of patients do not achieve seizure control.[1, 2] Furthermore, currently available AEDs are associated with a number of limitations, including a high prevalence of adverse events and interactions with other medications[2,,3]	
Dosage and Administration	The recommended starting dose is either 50 mg/day or 100 mg/day based on physician assessment of required seizure reduction versus potential side effects. The dose should be administered in two equally divided doses, once in the morning and once in the evening. Based on individual patient response and tolerability, the dose may be adjusted in the dose range of 50 mg/day to 200 mg/day.	
Renal Impairment	Mild	No dose adjustments
	Moderate	No dose adjustments
	Severe	Use with caution- monitor creatinine clearance
	End-stage renal disease patients undergoing dialysis	Not recommended
Hepatic impairment	Mild Moderate Severe	A 50 mg/day starting dose should be considered. A maximum daily dose of 150 mg administered in 2 divided doses is recommended for all stages of hepatic impairment
Contra-indications / Special precautions	Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the excipients <u>Suicidal ideation and behaviour</u> Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic drugs (AEDs), including brivaracetam, 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 any signs of suicidal ideation or behaviour emerge. <u>Lactose intolerance</u> Brivaracetam film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.	
Side Effects	Very common	Dizziness, somnolence
	Common	Influenza, decreased appetite, depression, anxiety, insomnia, irritability, vertigo, upper respiratory tract infections, cough, nausea, vomiting, constipation, fatigue

Monitoring	Pre-treatment assessment	Hepatic function Renal function Previous suicidal ideation and behaviours
	After commencing treatment	Annual hepatic function Annual renal function Signs of suicidal ideation and behaviours
	Actions to be taken: (for example)	
	Raise LFT	Withhold until discussed with specialist team.
	Creatinine clearance	If <30 mL/min, discuss with specialist team.
	Signs of suicidal ideation and behaviours	Discuss with GP/specialist team.

Drug Interactions (significant interaction as outlined in BNF, please see BNF and SPC for more detail)

Brivaracetam has the following interaction information:

Agent	Severity of interaction	Evidence for interaction	Detail
Carbamazepine	Moderate	Study	Carbamazepine decreases the concentration of brivaracetam.
Enzalutamide	Moderate	Theoretical	Enzalutamide is predicted to slightly decrease the exposure to brivaracetam.
Fosphenytoin	Moderate	Study	Fosphenytoin decreases the concentration of brivaracetam.
Phenytoin	Moderate	Study	Phenytoin decreases the concentration of brivaracetam.
Rifampicin	Moderate	Study	Rifampicin slightly decreases the exposure to brivaracetam. Manufacturer advises adjust dose.
St John's Wort	Moderate	Theoretical	St John's Wort is predicted to decrease the exposure to brivaracetam.

References

1. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med. 2000;342(5):314-9.
2. Goldenberg MM. Overview of drugs used for epilepsy and seizures: etiology, diagnosis, and treatment. P T. 2010;35(7):392-415.
3. Perucca E, Tomson T. The pharmacological treatment of epilepsy in adults. Lancet Neurol. 2011;10(5):446-56.
4. Briviact® SmPC. Accessed October 2017
5. BNF online – Sept 2017 update. Accessed October 2017

Appendix 1:

Effective Shared Care Agreement (ESCA)

Brivaracetam▼ oral formulations

For adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with severe refractory epilepsy warranting tertiary specialist input for patients who have tried three or more AEDs. Patient has used levetiracetam but has documentation of intolerance and patient is using a third line agent (perampanel, zonisamide, lacosamide or eslicarbazepine) which will be replaced with brivaracetam.

Please list the AED's agents that the patient has already tried prior to considering brivaracetam.
(Please see clinical letter for previous AEDs)

Antiepileptic agent	Dose	Duration	Reason for discontinuation

Please refer to BSSE APC formulary website for complete document.

BACK-UP ADVICE AND SUPPORT (To be completed by Tertiary Specialist team)

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

To be completed by the General Practitioner:

I agree to participate in this shared care agreement for the treatment of the below named patient with brivaracetam for the treatment of severe refractory epilepsy warranting tertiary specialist input for patient who has tried three or more AEDs.

General Practitioner
Name (please print)_____Signature _____Date_____

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant.

In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement.

GP Prescribing System	Read Code	Description		GP Prescribing System	Read Code	Description
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care