BNSSG Health Community's Traffic Light System
Shared Care Guidance

Please complete all sections.
Type in the grey shaded areas (deleting the prompts for information in each section).

Section 1: Heading

Trust: North Bristol NHS Trust

Specialty / Department: Neurosciences

Drug:Zonisamide

For the treatment / management of: Epilepsy

Section 2: Treatment schedule

Maintenance doses of zonisamide are usually in the range of 300-500mg daily given in one to two divided doses.

The safety and effectiveness in children and adolescents under 18 years have not been established therefore, use in these patients is not recommended

Caution must be exercised in treating patients with renal impairment, as there is limited information on use in such patients. Since zonisamide and its metabolites are excreted renally, it should be discontinued in patients who develop acute renal failure or where a clinically significant sustained increase in serum creatinine is observed.

Use in patients with hepatic impairment has not been studied. Therefore use in patients with severe hepatic impairment is not recommended. Caution must be exercised in treating patients with mild to moderate hepatic impairment.

When zonisamide treatment is to be discontinued, it should be withdrawn gradually. In clinical studies, dose reductions of 100 mg at weekly intervals have been used with concurrent adjustment of other anti-epileptic drug doses.

Please refer back to secondary care if advice is needed for unmanaged seizures.

Section 3: Monitoring

Prior to initation, secondary care will consider the patients renal function and liver function to allow safe dose initiation. Zonisamide should be used with caution in patients who have risk factors for nephrolithiasis, including prior stone formation, a family history of nephrolithiasis and hypercalcuia. Increasing fluid intake and urine output may help reduce the risk of stone formation, particularly those with predisposing risk factors. Renal and liver function should then be assessed subsequently by the General Practitioner if there are factors or symptoms that suggest deterioration.

In patients who develop the clinical signs of pancreatitis, it is recommended that pancreatic lipase and amylase levels are monitored. If pancreatitis is evident, in the absence of another cause it is recommended that discontinuation of zonisamide be considered and appropriate treatment initiated.

Drug plasma level monitoring is not necessary to optimise zonisamide therapy.
Patients should be monitored for common side effects such as somnolence, dizziness and anorexia.

Anti-epileptic drugs have been shown to cause a small increased risk of suicidal ideation and behaviour. Patients and care givers should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

Date approved: xx/xx/xxx

Date to be reviewed: xx/xx/xxxx

Section 4: Side-effects

It should be noted that zomisamide is a benzisoxazole derivative, which contains a sulphonamide group. Serious immune based adverse reactions that are associated with medicinal products containing a sulphonamide group include rash, allergic reaction and major haematological disturbances including aplastic anaemia, which very rarely can be fatal.

Common side effects include (1/10 patients) ;
Anorexia, irritability, depression, dizziness, somnolence, diplopia.

Other common side effects include;
nausea, diarrhoea, drowsiness, poor memory and attention and rash.

Serious dermatological reactions including Stevens-Johnson syndrome have been reported very rarely with zonisamide. Patients who develop skin reactions must be evaluated immediately and drug withdrawal and hospitalisation considered.

For a full list of side effects and the frequency at which they may occur please refer to the summary of product characteristics.

Where patients require discontinuation of therapy due to side effects please refer back to secondary care.

Section 5: Drug interactions

There is no data to suggest that zonisamide interacts to a clinically significant degree with any other medication. Caution should be used when CYP3A4 inducers are given co-committently with zonisamide due to the potential risk of a reduction in zonisamide levels. When these inducers are anti-epileptics that the zonisamide is an adjunct to,(e.g. phenytoin, carbamazepine, and phenobarbitone) the effect of any reduced plasma levels of zonisamide is not likely to be seen. If there is any dose alteration to a concommitent enzyme inducer, the consequential effect to the plasma levels of zonisamide should be considered, although unlikely to be clinically significant.

Other enzyme inducers that may be added into a patient's therapy (e.g. rifamicins) may lead to altered levels and, if co-administration is necessary, the patient should be closely monitored and the dose of zonisamide and other CYP3A4 substrates adjusted as needed.

Zonisamide has not been shown to significantly inhibit any of the CYP enzymes and is therefore not expected to affect the pharmacokinetics of other medicinal products via cytochrome P450-mediated mechanisms.

Section 6: Cautions and special recommendations

Zonisamide should not be used in patients who are hypersensitive to sulphonamides.

Very rare reports of agranulocytosis, aplastic anemia and pancytopenia have been seen in patients treated with zonisamide. Discontinuation of the medicinal product should be considered if any evidence of significant bone marrow depression develops.

Section 7: Advice to the patient

Any suspected side effects should be reported, particularly rashes (due to the risk of Stephen's Johnson Syndrome). There is also a rare risk of agranulocytosis and patients should be aware of the signs and symptoms of this developing.

There are no adequate data from the use of zonisamide in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. If pregnancy is suspected or desired the patient should see their GP.

No sudden discontinuation of anti-epileptic therapy should be undertaken as this may lead to breakthrough seizures which could have serious consequences.

Some patients may experience drowsiness or difficulty with concentration, particularly early in treatment or after a dose increase. Patients must be advised to exercise caution during activities requiring a high degree of alertness, e.g., driving or operating machinery.

Caution should be exercised if alcohol is taken in combination with zonisamide therapy, due to a possible additive sedative effect.

Section 8: Responsibilities for Secondary Care

1. Carry out any necessary blood monitoring prior to initiating therapy to confirm adequate renal and hepatic function.
2. Initiate therapy after discussion with the patient about treatment and possible side effects.
3. Prescribing responsibility remains with specialist for 3 months.
4. Seek agreement from Primary Care to continue prescribing under the shared care guideline
5. Respond promptly when requested to review patient and therapy.

Section 9: Responsibilities for Primary Care

1. Assume prescribing responsibility after 3 months of therapy.
2. Where deterioration of liver, renal or pancreatic function is suspected please request advice from secondary care regards drug dosing.
3. Ask the patient or care givers to report any changes in mood or behaviour. Respond to replies appropriately.
4. If side effects require dose reduction or discontinuation please contact secondary care for advice.

Section 10: Contact details

Name	Organisation	Telephone number	Fax number	E-mail address	Availability
Consultant Neurologist	NBT	0117 9701212 access via switchboard			
Neurology specialist registrar	NBT	0117 9701212 access via switchboard			

Section 11: Document details

Date prepared:	27/8/9
Prepared by:	Claire Daniels and Kirsty Newton
Date for review:	27/8/11
Document identification:	Zonisamide SCP NBT 0611
Approved by BNSSG D&TC:	June 2011

Section 12: Collaboration

This draft has been circulated to interested parties including Dr S Lhatoo Consultant Neurologist, Dr K Sierazdan Consultant Neurologist, Primary care representatives were also consulted regarding the draft forms of this guideline. NBT Formulary Pharmacist and other senior members of NBT Pharmacy Department.

Section 13: References

Please list references;
1- Summary of Product Characteristics - Zonisamide. www.emc.medicines.org.uk
2 - BNF 56- Zonisamide
3- Eisai Medicines information department