Doncaster & Bassetlaw Medicines Formulary

Section 4.8 Antiepileptics

Carbamazepine 100mg & 200mg Tablets
Carbamazepine 200mg & 400mg MR Tablets
Carbamazepine 100mg in 5ml Syrup
Carbamazepine 125mg & 250mg Suppositories
Sodium Valproate 100mg Crushable Tablets
Sodium Valproate 200mg and 500mg EC Tablets
Sodium Valproate 200mg, 300mg and 500mg MR Tablets
Sodium Valproate 150mg and 300mg MR Capsules
Sodium Valproate 200mg in 5ml Liquid
Sodium Valproate 300mg Injection
Phenytoin Sodium 25mg, 50mg and 100mg Capsules
Phenytoin Sodium 250mg in 5ml Injection
Phenytoin 30mg in 5ml Suspension
Phenytoin 50mg Chewable Tablets
Lamotrigine 25mg and 100mg Tablets
Lamotrigine 5mg, 25mg and 100mg Dispersible Tablets
Clonazepam 500 micrograms and 2mg Tablets

Midazolam 2.5mg in 0.5ml Solution
Midazolam 5mg in 1ml Solution
Midazolam 7.5mg in 1.5ml Solution
Midazolam 10mg in 2ml Solution

Drugs Used in Treating Status Epilepticus

Diazepam 5mg and 10mg Rectal Tubes
Diazepam 10mg in 2ml Emulsion Injection
Lorazepam 4mg in 1ml Injection
Phenytoin 250mg in 5ml Injection
Phenobarbitone 200mg in 1ml Injection

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Prescribing Guidance:

This section deals with the drug treatment of epilepsy in adults. See also NICE Guidance (CG137)

For the treatment of epilepsy in children, see NICE Guidance (CG20)

KEY: [UL] Unlicensed Preparation; Drug – first line choice; Drug – hospital only; Drug – Amber (TLS), Drug – Red (TLS), see http://medicinesmanagement.doncasterpct.nhs.uk/
Interactions with Anti-Epileptic Medicines

Interactions are common between antiepileptic agents. Consult the current BNF prior to commencing any new agents.

Combination Therapy

Combination therapy with two or more antiepileptic agents should usually only be used when monotherapy with different agents has proven ineffective.

Combination therapy enhances toxicity and drug interactions may occur.

Generic Prescribing

Further advice regarding switching of anti-epileptic medications can be found here.

Anti-Epileptic Agents in Pregnancy

There is an increased risk of teratogenicity associated with the use of antiepileptic agents. In view of the increased risk, women taking anti-epileptic therapy who may have become pregnant should be informed of the possible consequences, counselled and offered antenatal screening. Those who wish to become pregnant should be warned of the teratogenic risks and referred to an appropriate specialist for advice.

Secondary Generalised Tonic-Clonic or Partial Seizures

First-line – Lamotrigine
Alternative – Carbamazepine, Phenytoin or Sodium Valproate

Primary Generalised or Absence Seizures

Sodium Valproate

Myoclonic Jerks

First-line – Sodium Valproate
Alternative – Clonazepam

Newer Anti-Epileptics/Second Line Agents

The following anti-epileptic agents are available for use only on the advice of an Epilepsy Specialist or Consultant Neurologist:
- Eslicarbazepine

Prescribing outside this formulary should only take place via a New Product Request.
- Topiramate
- Gabapentin
- Vigabatrin: this drug is restricted to use in infantile spasms (West’s syndrome) and only with then prescribed with close monitoring of visual fields, due to risks of retinopathy (movement disorders and MRI abnormalities have also been reported).

- Phenobarbitone
- Primidone
- Pregabalin
- Levetiracetam
- Oxcarbazepine
- Ethosuximide
- Tiagabine
- Clobazam
- Rufinamide
- Lacosamide
- Zonisamide

For advice on dosing, see the current edition of the BNF, or contact a pharmacist as appropriate.

The drugs are colour coded to reflect the local traffic light status. Further details are available from the Doncaster PCT website.

**Carbamazepine**

This drug has historically been seen as the drug of choice for simple and complex partial seizures and for tonic-clonic seizures secondary to a focal discharge. However, see also prescribing guidance for lamotrigine.

Target plasma concentration for optimum response: 20 to 50 micromol/litre.

It is unnecessary to take routine levels at normal doses unless non-compliance, overdose or sub-therapeutic dosing is suspected due to the wide variation in plasma levels.

Side effects such as blurred vision, dizziness and unsteadiness are dose-related and may occur although serum levels are within the therapeutic range.

The use of modified-release carbamazepine preparations can limit these side effects.

Rectal dosage: 125mg suppositories ≡ 100mg tablets or syrup

Licensed for short term use only for seven days if patient unable to take oral therapy. Maximum dose – 1g daily in 4 divided doses.
CSM WARNING: Blood, Hepatic or Skin Disorders

Patients or their carers should be told how to recognise signs of blood, liver or skin disorders, and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding develop.

Leucopenia which is severe, progressive or associated with clinical symptoms requires withdrawal.

**Lamotrigine**

The authors of a recent large multicentre study concluded that Lamotrigine is clinically better than Carbamazepine, the standard drug treatment, for time to treatment failure outcomes and is therefore a cost-effective alternative for patients diagnosed with partial onset seizures, see: [NIHR Health Technology Assessment Website](https://www.nets.nhs.uk/hta/)

It has however, been associated with serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (rarely, with fatalities) – especially in children. Most rashes occur in the first eight weeks of treatment. As a result, BNF dosing schedules should be strictly adhered to.

**Sodium Valproate**

Sodium Valproate is indicated for all forms of epilepsy and is the drug of choice for myoclonic jerks and absence seizures.

The authors of a recent large multicentre study concluded that Valproate is better tolerated than Topiramate and more efficacious than Lamotrigine, and should remain the drug of first choice for many patients with generalised and unclassified epilepsies: see [NIHR Health Technology Assessment Website](https://www.nets.nhs.uk/hta/).

An intravenous injection is available for continuation of therapy when the oral route is not available.

Many drugs interact with Sodium Valproate – see the most current version of the [BNF](https://www.gov.uk/government/organisations/medicines-licensing-agency) for details.

**Warning:**

Raised liver enzymes are not uncommon during Valproate treatment and are usually transient, patients should be reassessed clinically and liver function including prothrombin time monitored until they return to normal.

Withdraw treatment if the following occur, vomiting, anorexia, jaundice, drowsiness or loss of seizure control, confusion, lethargy or aggression or hyperactivity.

Leucopenia and pancytopenia have also been reported.

**Advice for Prescribers Regarding the Risk of Abnormal Pregnancy Outcomes**

Prescribing outside this formulary should only take place via a New Product Request.
Phenytoin

Phenytoin is effective in tonic-clonic and partial seizures.

Phenytoin has a narrow therapeutic index. Small increases in dose can produce large rises in plasma concentrations. Dosage should be increased by no more than 25 to 50mg/daily with monitoring of plasma levels, dosage should be adjusted not more frequently than every 2 to 4 weeks.

N.B. Phenytoin 90mg (in 15ml of suspension or in chewable tablets) may be considered to be approximately equivalent in terms of therapeutic effect to Phenytoin Sodium 100mg (in capsules, tablets or injection), but nevertheless, care is needed in making changes.

Phenytoin may cause coarse facies, acne, hirsutism and gingival hyperplasia and should be used with caution in young patients.

Phenytoin may cause folate deficiency and an annual FBC is recommended.

Patients and carers should be advised to recognise signs of skin or blood disorders. They should seek medical advice if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding occur.

Many drugs interact with phenytoin (including oral contraceptives) see advice above. Phenytoin also interacts with enteral feeds when administered via feeding tubes. Here it should be administered as a single daily dose, where possible and enteral feeds should be stopped two hours before and restarted two hours after dosing.

CSM Warning: Blood, Hepatic or Skin Disorders

Patients or their carers should be told how to recognise signs of blood, liver or skin disorders, and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding develop.

Leucopenia which is severe, progressive or associated with clinical symptoms requires withdrawal.

Clonazepam

Clonazepam is occasionally used in tonic-clonic epilepsy and in partial seizures but its sedative effects may be prominent. It is also used second line for myoclonic jerks.

Items for Restricted Prescribing:

Sodium Valproate 500mg and 1g sachets (Episenta) are available where a MR liquid preparation is required. They are restricted to use in Paediatrics.
Drugs Used in the Treatment of Status Epilepticus (within DBH)

See also NICE Clinical Guideline no. 20: Epilepsy in Children and Young People and SIGN Guideline 70: Diagnosis and Management of Epilepsy in Adults. Also available, Guidance for Prescribing Rectal Diazepam or Buccal Midazolam in Children and Young People

Major status epilepticus should be treated with Lorazepam 4mg IV over at least 2 minutes into a large vein.

IM injection is not recommended due to slow and erratic absorption.

Diazepam 10mg rectally should be considered if gaining intravenous access is likely to take more than 10 to 15 minutes. Onset of action is slower than IV Lorazepam.

Monitor blood glucose. If hypoglycaemic administer 50ml of 50% glucose. Give parenteral Thiamine (as 2 pairs of ampoules of Pabrinex) if there are indicators of alcohol abuse or impaired nutritional status.

Repeat Lorazepam 4mg IV (over at least 2 minutes) if no response after 10 minutes. Observe for respiratory depression.

IF STATUS PERSISTS:

Give Phenytoin IV as a loading dose, 18mg/kg (at a rate of 50mg/minute), with ECG and blood pressure monitoring. Continue with a maintenance dose of 100mg every 6 to 8 hours.

Phenytoin can be given undiluted (preferred method) or as an infusion, further diluted in 50 to 100ml Sodium Chloride 0.9% to a final concentration not exceeding 10mg/ml, over one hour (if an infusion is given ensure a separate filter with pore size 0.2 to 0.5 microns is used). Complete administration within 1 hour of preparation.

IM injection is NOT recommended due to slow and erratic absorption. It can cause local irritation at the injection site, flush well with saline after administration.

If status persists seek expert advice. Admission to DCC may be necessary for administration of Phenobarbitone or general anaesthesia. Administration of phenobarbitone and indeed general anaesthesia should only be performed in the presence of an appropriately qualified individual, ie. an anaesthetist.

An IPOC for use in the management of status epilepticus in children within Doncaster and Bassetlaw hospitals is available.