Epilepsy - Treatment in Adults

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1.0	2004	Bridget Coleman Dr V. Stephenson	OFF LINE	
2.0	March – Dec 2014	Dr C. Lane Aarti Nandani Dr K. Sidle	LIVE	 All areas in previous version reviewed and updated. Inclusion of following new sections: Management of epilepsy during labour Therapeutic Drug Monitoring Administration via enteral tubes and non-enteral routes Patient advice and counselling Removal of: Seizure type and drug selection Maintenance anticonvulsants

Version Control Sheet

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Criteria for use

This guideline is intended to aid the assessment and management of adult patients admitted to the Whittington with known epilepsy and convulsive status epilepticus.

It also provides guidance on therapeutic drug monitoring, administration of anti-epileptic drugs (AEDs) via enteral feeding tubes and when the patient is nil-by mouth. Please Liaise with neurology team for specific advice.

It does not cover first fits and their management.

Background/ introduction

Epilepsy is a common neurological disorder characterised by recurring seizures. Different types of epilepsy have different causes. Epilepsy has been estimated to affect between 362,000 and 415,000 people in England. Incidence is estimated to be 50 per 100,000 per year and the prevalence of active epilepsy in the UK is estimated to be 5-10 cases per 1000. Two-thirds of people with epilepsy have their epilepsy controlled satisfactorily with anti-epileptic drugs (AEDs) and approximately 50% of newly diagnosed patients become seizure-free within one year of starting treatment with an AED.

General Principles of Epilepsy Management

- Establish a definite diagnosis of epilepsy prior to commencing treatment:
 - Conditions potentially mimicking epilepsy include syncope, transient ischaemic attacks (TIA), hypoglycaemia, pseudoseizures, and drug withdrawal.
 - $\circ\,$ Underlying causes of epilepsy include tumour, haemorrhage, abscess and alcohol excess

Anti-epileptic treatment is usually commenced if a patient has had more than one attack within 12 months and should ALWAYS involve discussion with a Neurologist

- Anti-epileptic drugs (AEDs) should **NOT** be introduced unless there is a clear history of epilepsy (i.e. repeated, non-provoked seizures with a good witness history)
- Choice of drug depends on:
 - Seizure type and epilepsy syndrome
 - Patient preference including lifestyle factors
 - o Age
 - Childbearing potential
 - Other comorbidities
 - Likely interactions with concomitant medication

• Formulations available

- Commence with single drug treatment and introduce gradually. Maximise single drug treatment before changing to another AED. Multiple drug therapy should be avoided if at all possible and only considered when all appropriate drugs have been tried singly at the maximum tolerated dose.
- If a patient has known epilepsy and has been admitted following increased seizure frequency with a provoking factor e.g. infection, there is no reason to alter the drug regimen. Discuss each case with the Consultant Neurologist and consider giving clobazam 10mg bd for three days in these circumstances and discharging the patient, provided they are well enough and have adequate support at home.
- Regular blood test monitoring of AEDs is not recommended as routine and should only be performed if clinically indicated (refer to *Therapeutic Drug Monitoring*)
- Withdrawal of AEDs is usually implemented gradually over at least 2-3 months (sometimes longer) and should be performed under the guidance of a Consultant Neurologist
- Ensuring patients receive their AED in a timely fashion is paramount. Omission of a dose of AED is classed by the NPSA as risking significant or catastrophic long-term patient impact.
- Out-of-hours, if patients have not brought in their own medication and there is no-one available to bring in medication, check the Emergency Drug Cupboard (list on intranet; cupboard located on Nightingale ward). If you are unable to locate the necessary medication, contact the on-call pharmacist via switchboard.
- Where patients require medication administration via enteral feeding tubes or are NBM, alternatives are available (refer to Administration via enteral tube and non-enteral routes)

> Status epilepticus

Status epilepticus is defined as recurring seizures, without recovery of consciousness, for 30 minutes or more. It is important to distinguish genuine status from pseudoseizures. However, this can be difficult and if unsure, treat as status.

In practice a patient should be treated as being in status if their seizure has lasted more than five minutes (and their usual seizures are shorter).

Get the Anaesthetist and Neurologist involved EARLY.	
Set the Andesthetist and Neurologist involved LARET.	

General Measures		
Early Status	1 st Stage (0-10 minutes)	
	 Ensure patency of airway and resuscitate. if airway not patent call anaesthetist. Administer oxygen Assess cardiorespiratory function Establish intravenous access 	
	2 nd stage (0-30 minutes)	
	 Institute regular monitoring (see below*). 	
	• Emergency AED therapy (refer to Emergency AED therapy for convulsive status epilepticus table on page 6)	
	 Emergency investigations (see below^{**}) 	
	 Administer glucose (50ml of 50% solution) and/or intravenous Pabrinex if any suggestion of alcohol abuse or impaired nutrition 	
	 Assess for and treat acidosis 	
	Consider the possibility of non-epileptic status	
	Alert anaesthetist and ITU	
Established	3 rd stage (0-60 minutes)	
status	Establish aetiology	
	Identify and treat medical complications	

Refractory status	4 th stage (0-90 minutes)
Status	Transfer to intensive care
	Establish intensive care and EEG monitoring
	Initiate long-term, maintenance AED therapy (discuss with
	neurologist)

*Monitoring

- Regular neurological observations (minimum of 5 minute intervals) and measurements of pulse, blood pressure, temperature, sats, ECG, biochemistry, blood gasses, clotting, blood count and drug levels
- Blood pressure and cardiac monitoring is required when administering phenytoin infusion due the risk of hypotension and arrhythmias
- Patients require the full range of ITU facilities and care should be shared between anaesthetist and neurologist

**Emergency investigations

- CBG
- Bloods for FBC, glucose, U&Es, LFTs, bone profile, magnesium, clotting and AED levels
- 5ml serum and 50ml of urine samples should be saved for future analysis, especially if cause of status epilepticus is uncertain.
- CXR to evaluate for possible aspiration
- Brain imaging and LP may need to be considered depending on clinical picture

Emergency AED therapy for convulsive status epilepticus

Premonitory stage (pre- hospital)	 Buccal midazolam 10mg OR Rectal diazepam 10-20mg, repeated ONCE after 15 minutes if status continues. 	
Early status*	Lorazepam (intravenous) 0.1mg/kg (usually a 2-4mg bolus into a large vein), repeated ONCE after 10-20 minutes. (Dilute dose with an equal volume of 0.9% Normal Saline or Water for Injection pre-administration) OR	
	 Diazepam (intravenous) 10mg over 2 minutes into a large vein, repeated ONCE if necessary Contraindicated in patients allergic to egg or soyabean Use diazepam emulsion (Diazemuls) if available as this 	

	1			
	causes less injection site irritation than diazepam			
	solution			
	Administer a maximum of TWO doses of IV			
	lorazepam/diazepam			
	Give usual AED medication if already on treatment			
	For sustained control or if seizures continue, treat as below			
Established	Phenytoin infusion (loading dose):			
status	 Patient not usually on phenytoin: ► Loading dose at 			
Slalus	20mg/kg (maximum 2g).			
	• OR			
	 Patient already on phenytoin: ► loading dose 			
	should only be administered if the patient is sub-			
	therapeutic on blood levels			
	 Add to 50-250mls 0.9% Normal Saline (maximum 			
	concentration 10mg/ml)			
	 Administer via a syringe pump or volumetric infusion 			
	pump through a large vein or central line at a rate not			
	exceeding 1mg/kg/minute (maximum 50mg/minute)			
	• The full dose should be given within ONE hour of			
	preparation			
	 Give through a 0.2micron filter 			
	• Monitor ECG and blood pressure. Reduce infusion			
	rate if hypotension or bradycardia occur.			
	 Take levels 18-24 hours post-loading (refer to 			
	Therapeutic Drug Monitoring)			
	 Maintenance dose of 100mg 6-8 hourly, adjusted to 			
	plasma phenytoin level			
Refractory	General anaesthesia with ONE of:			
status**				
oluluo	Thiopental sodium			
	Midazolam			
	Propofol (unlicensed)			
	Anaesthetic continued for 12-24 hours after the last clinical or			
	electrographic seizure, then dose tapered			
	erm manufacturing issue with intravenous lorazepam, therefore n first-line until this issue is resolved			

**In the above scheme, the refractory stage (general anaesthesia) is reached 60/90 minutes after the initial therapy

> Management of Epilepsy Patients During Labour

- Up to 5% of women with epilepsy will have a tonic-clonic seizure during labour or the puerperium, risking maternal hypoxia, fetal hypoxia and acidosis
- Seizures in labour should be terminated as soon as possible using intravenous lorazepam or diazepam. If seizures persist, manage as for status epilepticus.
- Ensure that all patients with known epilepsy have intravenous access during labour and either lorazepam or diazepam readily to hand in case of seizure
- If there is any doubt whether a seizure in labour is due to eclampsia or epilepsy, then in addition to intravenous lorazepam/diazepam, a slow intravenous bolus of 4g (16mmol) magnesium sulphate over 5 -10minutes followed by 1g (4mmol)/hour for 24 hours is recommended.



> Therapeutic Drug Monitoring

- Regular blood test monitoring in adults is not recommended as routine, and should be done only if clinically indicated.
- Indications for monitoring of AED blood levels are:
 - Detection of non-adherence to the prescribed medication
 - Suspected toxicity
 - Adjustment of phenytoin dose
 - Management of pharmacokinetic interactions (for example, changes in bioavailability, changes in elimination, and co-medication with interacting drugs)

- Formulation changes
- Specific clinical conditions, for example, status epilepticus, organ failure and certain situations in pregnancy
- Symptoms of toxicity include:
 - Ataxia
 - o Diplopia
 - Confusion
 - Nausea and vomiting
- Do not routinely monitor AED levels during pregnancy. If seizures increase or are likely to increase, monitoring AED levels (particularly levels of lamotrigine and phenytoin, which may be particularly affected in pregnancy) may be useful when making dose adjustments.
- Where blood level monitoring is indicated, plasma samples should not be obtained until steady-state concentrations of drug have been achieved. Levels taken before steady-state has been achieved can provide misleading results and result in inappropriate dosing decisions. In certain cases, it is however appropriate to measure drug levels before steady state e.g. severely ill patients, suspected toxicity, phenytoin etc.
- The table below provides information on therapeutic drug monitoring in **adults.** Note that pharmacokinetic parameters can vary significantly between children and adults and therefore **this information should not be applied to the paediatric population**.

Medication	Ideal sampling time	Therapeutic range	Comments
Carbamazepine	2-4 weeks after initiation of therapy Pre-dose (trough)	4-12mg/L (Symptoms of toxicity often seen at levels >9mg/L therefore a range of 4-8mg/L may be preferred)	
Ethosuximide	At least 10-days after initiation Pre-dose (trough) though not critical due to long half-life	40-100mg/L	Incidence of adverse effects is relatively low and does not correlate well with plasma concentrations. Plasma levels used primarily to evaluate potential for clinical response and compliance.
Lamotrigine	3-15 days post-initiation of therapy depending on co-	6-16mg/L	TDM particularly important in pregnancy

	medication (specific advice provided in summary of product characteristics (SPC)) Pre-dose (trough)		when clearance is increased and there is a decline in levels resulting in loss of seizure control necessitating higher doses. Similarly, close monitoring required post-partum when clearance normalises and toxicity can occur.
Phenobarbital	2-3 weeks post-initiation Oral: Pre-dose (trough) though not critical due to long-half life IV: At least 2 hours post dose	15-40mg/L	Concentrations in excess of 100 to 150mg/L are potentially lethal.
Phenytoin	 Levels should be taken: Within 2-3 days of treatment initiation (18-24 hours post-loading) 3-5 days after first level to allow dose adjustment If little change between first and second levels, increase monitoring interval to once weekly in acute clinical setting. In stable patients requiring long-term therapy monitor levels at 3-12 month intervals as advised by Neurologist 	10-20mg/L (5-10mg/L may be therapeutic in some patients)	Phenytoin levels require careful interpretation in patients with hypoalbuminaemia, renal failure or taking valproic acid – discuss such patients with your ward pharmacist for further advice.
Sodium Valproate (valproic acid)	4-days post-initiation of therapy Pre-dose (trough)	50-100mg/L (concentrations >100mg/L often required in patients with partial seizures)	

> Administration via enteral tube and non-enteral routes

- Administration of medication to patients with swallowing difficulties or limited GI access often presents difficulties
- The table below provides some guidance on administration of commonly prescribed AEDs through enteral tubes and non-enteral routes, however the ward or on-call pharmacist should always be contacted for advice in this regard.
- There is limited information available in respect of intrajejunal administration of the majority of AEDs and patients should be closely monitored for increased side-effects or loss of efficacy.
- Under no circumstances should modified release preparations be crushed and administered; information about alternative formulations is provided in the table below.

Patient's Usual Medication	Enteral tube administration	Alternative routes (non-enteral)
Carbamazepine (modified or normal release tablets)	 Carbamazepine liquid 100mg/5ml Dilute with an equal volume of water prior to administration (reduces adsorption to enteral tube) No dose conversion required however, if total daily dose exceeds 400mg, give in 4 divided doses 	 Carbamazepine suppositories 125mg suppository approximately equivalent to 100mg tablet; max 1g daily in 4 divided doses Maximum licensed duration of treatment with suppositories = 7 days
Clobazam	 Consider an alternative drug where possible Disperse tablets in water immediately prior to administration Clobazam suspension 5mg/5ml and 10mg/5ml (unlicensed preparation) – check with pharmacy to confirm availability 	• Nil
Clonazepam tablets	Disperse tablets in 10mls water immediately prior to administration	• Nil
Gabapentin	Open capsule and disperse contents in water immediately prior	• Nil

capsules	to administration	
Lamotrigine tablets	 Use dispersible tablet formulation Disperse dispersible tablets in 10mls water immediately prior to administration 	• Nil
Levetiracetam tablets	 Levetiracetam 100mg/ml solution No dose conversion required 	 Levetiracetam concentrate for intravenous infusion 100mg/ml No dose conversion required
Phenobarbital	Phenobarbital 50mg/5ml solution	 Parenteral route available however usually reserved for acute treatment. Intramuscular phenobarbital may be given as a substitute for oral Phenobarbital on a mg for mg basis. Discuss with Consultant Neurologist.
Phenytoin sodium capsules and tablets	 Phenytoin base 90mg/5ml liquid Convert dose using formula: 100mg phenytoin sodium = 90mg phenytoin base Stop enteral feeding 2 hours before dose and recommence 2 hours after dose; plasma level monitoring recommended whilst receiving enteral feeds and following discontinuation Extremely poor absorption via jejunal route; plasma concentration monitoring required If administering via jejunal route, ensure suspension is diluted as phenytoin suspension is hyperosmolar and can cause diarrhoea through this route. 	 Phenytoin sodium injection If previously on liquid, convert dose using formula: 100mg phenytoin sodium = 90mg phenytoin base Administer total daily dose in three to four divided doses by slow IV injection
Valproate (sodium) (immediate release and modified release tablets)	 100mg Epilim tablets can be crushed/shaken in 10mls water immediately prior to administration Sodium Valproate 200mg/5ml liquid – dilute with water immediately prior to administration Give in 2 divided doses 	 Intravenous infusion Same as oral dose

For information on other AEDs contact the ward or on-call pharmacist.

> Surgical Patients and other elective NBM situations

Reason patient is NBM	Guidelines		
Emergency surgery	In general, it is strongly advisable to continue a patient's AEDs as per usual, but ensure they are taken with sufficient water and that they do not stick in the back of the throat prior to intubation		
	Always liaise with the surgeon and anaesthetist about whether tablets can be given, as even in patients NBM with NG aspirate it may be possible to give the drugs.		
Elective surgery	Advice as above, but it is best to consider this issue at the pre- assessment clinic so that there is a clear plan to minimize the number of missed doses of medication.		
Upper gastrointestinal endoscopy	Patient can take their usual medications with a small amount of water up to 1 hour before the procedure.		
Abdominal ultrasound	Patients can take their usual medications, but only with water (i.e. not with milk or tea etc.).		



Please see Whittington Hospital NHS Trust Guideline:

'Nil By Mouth (Nbm) Peri-Operative Medicines Use Guideline'

http://whittnet/document.ashx?id=5742

Patient Advice and Counselling

Driving (see driving and epilepsy leaflet on intranet)

- Patients who have had a first or single epileptic seizure must not drive for 6 months (5 years in the case of large goods or passenger carrying vehicles) after the event; driving may then be resumed, provided the patient has been assessed by a specialist as fit to drive because no abnormality was detected on investigation.
- Patients with epilepsy may drive a motor vehicle (but not a large goods or passenger carrying vehicle) provided that they have been seizure-free for one year or, if subject to attacks only while asleep, have established a 3-year

period of asleep attacks without awake attacks. Those affected by drowsiness should not drive or operate machinery.

 Guidance issued by the Drivers Medical Unit of the Driver and Vehicle Licensing Agency (DVLA) recommends that patients should be advised not to drive during medication changes or withdrawal of antiepileptic drugs, and for 6 months afterwards.

Contraception and Pregnancy

- Women of child-bearing potential who take antiepileptic drugs should be given contraceptive advice (refer to current version of BNF). Some antiepileptic drugs can reduce the efficacy of hormonal contraceptives, and the efficacy of some antiepileptics may be affected by hormonal contraceptives.
- Women who want to become pregnant should be referred to a specialist for advice in advance of conception.

Other Lifestyle advice

- Avoid high-risk sports such as rock climbing or swimming and patients should shower rather than bath, particularly if no one else is in the house.
- Avoid provoking factors such as sleep deprivation and excessive alcohol consumption.

> Further information

The following are useful resources for both patients and health professionals:

- Epilepsy Action website: <u>http://www.epilepsy.org.uk/</u>
- Epilepsy Society website: <u>http://www.epilepsysociety.org.uk/</u>

> Contacts (inside and outside the Trust including out-of-hours contacts)

- Consultant Neurologist (email <u>whh-tr.NeurologyInternalReferrals@nhs.net</u> OR contact via switch Mon-Fri 9-5. Out of hours contact oncall neurology at Queen Square via switch)
- Ward Pharmacist
- Medicines Information (ext. 5021)

Out-of-hours:

- Queen's Square on-call Neurology Registrar (via switchboard)
- On-call pharmacist (via switchboard)

References (evidence upon which the guideline is based)

- NICE (2012) The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (Clinical guideline 137) London: NICE [online] Available from: <u>http://publications.nice.org.uk/the-</u> epilepsies-the-diagnosis-and-management-of-the-epilepsies-in-adults-andchildren-in-primary-and-cg137
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- 3) Meierkord H. *et al* (2010) EFNS guideline on the management of status epilepticus in adults. *European Journal of Neurology*, 17: 348-355
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- UKMI (2010) NPSA Rapid Response Report: Reducing Harm from omitted and delayed medicines in hospital – A tool to support local implementation. [online] Available from: <u>http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Patient-Safety/NPSA-Rapid-Response-Report-Reducingharm-from-omitted-and-delayed-medicines-in-hospital-A-tool-to-support-localimplementation/ [accessed 07/04/12]
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- 10) SIGN (2003, updated 2005) Diagnosis and Management of Epilepsy in Adults, Guideline No. 70
- 11) Dollery C (1999) Therapeutic Drugs, 2nd ed. Churchill Livingstone, Edinburgh

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	Does the procedural document affect one group less or more favourably than another on the basis of:		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	Nationality	No	
	• Gender	No	
	Culture	No	
	Religion or belief	No	
	Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	 Disability - learning disabilities, physical disability, sensory impairment and mental health problems 	No	
2.	Is there any evidence that some groups are affected differently?	No	
3.	If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?	N/A	
4.	Is the impact of the procedural document likely to be negative?	No	
5.	If so can the impact be avoided?	N/A	
6.	What alternatives are there to achieving the procedural document without the impact?	N/A	
7.	Can we reduce the impact by taking different action?	N/A	

Checklist for the Review and Approval of Procedural Document

	Title of document being reviewed:	Yes/No	Comments
1.	Title		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	Rationale		
	Are reasons for development of the document stated?	Yes	
3.	Development Process		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	Content		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	Evidence Base		
	Are key references cited in full?	Yes	
	Are supporting documents referenced?	Yes	
6.	Approval		
	Does the document identify which committee/ group will approve it?	Yes	
7.	Dissemination and Implementation		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	Document Control		
	Does the document identify where it will be held?	Yes	
9.	Process to Monitor Compliance and		

	Title of document being reviewed:	Yes/No	Comments
	Effectiveness		
	Are there measurable standards or KPIs to support the monitoring of compliance with and effectiveness of the document?	Yes	
	Is there a plan to review or audit compliance with the document?	Yes	
10.	Review Date		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	Overall Responsibility for the Document		
	Is it clear who will be responsible for co- ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval						
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval						
Name	Date					
Signature						
Relevant Com	mittee Approval					
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.						
Name		Date				
Signature						
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes						
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee						
Name		Date				
Name of Committee		Name & role of Committee Chair				
Signature						

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Asses s/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report ? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	Lead	ΤοοΙ	Frequency	Reporting arrangements
Therapeutic drug monitoring done for appropriate indication	Consultant Neurologist	Audit	Biennial	Neurology MDT
Status epilepticus managed as per protocol	Consultant Neurologist	Audit	Annual	Neurology MDT
Any missed doses of anti- epileptics	Consultant Neurologist	Audit	Annual	Neurology MDT
Documentation of patient advice and counselling following changes to drug therapy	Consultant Neurologist	Audit	Biennial	Neurology MDT