APPENDIX K

Pharmacological Management

Table 1 AED options by seizure type

Seizure type	First-line AEDs	Adjunctive AEDs	Other AEDs that may be considered	Do not offer AEDs (may worsen seizures)
Generalised tonic–clonic	Carbamazepine Lamotrigine Oxcarbazepine* Sodium valproate	Clobazam* Lamotrigine Levetiracetam Sodium valproate Topiramate		(if there are absence or myoclonic seizures, or if JME suspected) Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Tonic or atonic	Sodium valproate	Lamotrigine*	Rufinamide Topiramate*	Carbamazepine Gabapentin Oxcarbazepine Pregabalin Tiagabine Vigabatrin
Absence	Ethosuximide Lamotrigine* Sodium valproate	Ethosuximide Lamotrigine* Sodium valproate	Clobazam* Clonazepam Levetiracetam* Topiramate* Zonisamide*	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Myoclonic	Levetiracetam* Sodium valproate Topiramate*	Levetiracetam Sodium valproate Topiramate*	Clobazam* Clonazepam Piracetam Zonisamide*	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Focal with/without secondary generalisation	Carbamazepine Lamotrigine Levetiracetam Oxcarbazepine Sodium valproate	CarbamazepineClobazam* Gabapentin* Lamotrigine Levetiracetam Oxcarbazepine Sodium valproate	Eslicarbazepine acetate* Lacosamide Phenobarbital Phenytoin Pregabalin* Tiagabine	

* At the time of publication ([month year]), this drug did not have UK marketing authorisation for this indication and/or population (please see appendix E for specific details about this drug for this indication and population). Informed consent should be obtained and documented.

		Topiramate	Vigabatrin Zonisamide*	

Table 2 AED options by epilepsy syndrome

Epilepsy syndrome	First-line AEDs	Adjunctive AEDs	Other AEDs	Do not offer AEDs (may worsen seizures)
Childhood absence epilepsy	Ethosuximide Lamotrigine* Sodium valproate	Ethosuximide Lamotrigine Sodium valproate	Clobazam* Clonazepam Levetiracetam* Topiramate* Zonisamide*	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Juvenile absence epilepsy	Ethosuximide Lamotrigine* Sodium valproate	Ethosuximide Lamotrigine Sodium valproate	Clobazam* Clonazepam Levetiracetam* Topiramate* Zonisamide*	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Juvenile myoclonic epilepsy	Lamotrigine* Levetiracetam* Sodium valproate Topiramate*	Lamotrigine* Levetiracetam Sodium valproate Topiramate*	Clobazam* Clonazepam Zonisamide*	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Epilepsy with generalised tonic–clonic seizures only	Carbamazepine Lamotrigine Oxcarbazepine* Sodium valproate	Clobazam* Lamotrigine Levetiracetam Sodium Valproate Topiramate		
Idiopathic Generalised Epilepsies	Lamotrigine* Sodium valproate Topiramate*	Lamotrigine* Levetiracetam* Sodium valproate Topiramate*	Clobazam* Clonazepam Zonisamide*	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Infantile spasms	Steroid or (prednisolone or tetracosactide*) vigabatrin (when infantile spasms not due			

* At the time of publication ([month year]), this drug did not have UK marketing authorisation for this indication and/or population (please see appendix E for specific details about this drug for this indication and population). Informed consent should be obtained and documented.

	to tuberous sclerosis)Vigabatrin (when infantile spasms due to tuberous sclerosis)			
Benign epilepsy with centrotemporal spikes	Carbamazepine Lamotrigine Levetiracetam Oxcarbazepine Sodium valproate			
Panyiotopoulos syndrome and late-onset childhood occipital epilepsy (Gastaut type)	Carbamazepine* Lamotrigine* Levetiracetam* Oxcarbazepine* Sodium valproate			
Dravet syndrome	Sodium valproate Topiramate*	Clobazam* Stiripentol		Carbamazepine Gabapentin Lamotrigine Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Continuous spike wave of slow sleep	Referral to a tertiary epilepsy specialist			
Lennox–Gastaut syndrome	Sodium valproate	Lamotrigine	Rufinamide Topiramate Felbamate *	Carbamazepine Gabapentin Oxcarbazepine Pregabalin Tiagabine Vigabatrin
Landau–Kleffner syndrome	Referral to a tertiary epilepsy specialist			
Myoclonic-astatic epilepsy	Referral to a tertiary epilepsy specialist			

* At the time of publication ([month year]), this drug did not have UK marketing authorisation for this indication and/or population (please see appendix E for specific details about this drug for this indication and population). Informed consent should be obtained and documented.

Licensing indications

Detailed below are drugs that have been recommended but which do not currently have licensed indications for these seizures types or syndromes or particular populations.

Table 3 Licensing indications of the guideline AEDs

Seizure type/syndrome	Drug	Details of licensing
Treatment of refractory focal seizures	**Clobazam**	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). This was because of insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
	Gabapentin	At the time of publication, gabapentin did not have UK marketing authorisation for use in children younger than 6 years and at doses over 50 mg/kg daily in children younger than 12 years (BNFC). The use of gabapentin was not recommended in this age group owing to the lack of sufficient supporting data (SPC).
	Eslicarbazepine acetate	At the time of publication, eslicarbazepine acetate did not have UK marketing authorisation for use in children younger than 18 years. It was not recommended owing to a lack of data on safety and efficacy (SPC).
	Pregabalin	At the time of publication, pregabalin did not have UK marketing authorisation for use in children (BNF). Pregabalin was not recommended for use in children younger than 12 years and adolescents (12–17 years) owing to insufficient data on safety and efficacy (SPC).
	Zonisamide	At the time of publication, zonisamide did not have UK marketing authorisation for use in children younger than 18 years owing to insufficient data on safety and efficacy (SPC).
GTC	**Oxcarbazepine**	At the time of publication,

		oxcarbazepine did not have UK marketing authorisation for GTC seizures (BNF). It had authorisation for focal with or without secondarily generalised tonic–clonic seizures (BNF).
	Clobazam	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). There was insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
Absence seizures	**Clobazam**	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). This was because of insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
	Lamotrigine	At the time of publication, lamotrigine had UK marketing authorisation for monotherapy of typical absence seizures for those aged 2–12 years only. There was not authorisation outside of this age range (BNF).
	Levetiracetam	At the time of publication, levetiracetam did not have UK marketing authorisation for use in absence seizures but had authorisation for focal seizures with or without secondary generalisation and adjunctive therapy for myoclonic and GTC seizures(BNFC).
	Topiramate	At the time of publication, topiramate did not have UK marketing authorisation for use in absence seizures but had authorisation for focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome(BNF).
	Zonisamide	At the time of publication, zonisamide did not have UK

		marketing authorisation for use in absence seizures but had authorisation for adjunctive therapy for adult patients with partial seizures, with or without secondary generalisation (BNF)
Myoclonic seizures	**Clobazam**	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). This was because of insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
	Levetiracetam	At the time of publication, levetiracetam did not have UK marketing authorisation for monotherapy use in myoclonic seizures but had authorisation for monotherapy and adjunctive treatment of focal seizures with or without secondary generalisation and adjunctive therapy for myoclonic and GTC seizures (BNFC).
	Topiramate	At the time of publication, topiramate did not have UK marketing authorisation for use in myoclonic seizures. It had authorisation for monotherapy and adjunctive treatment of focal seizures and GTC seizures and as adjunctive treatment for seizures associated with Lennox–Gastaut syndrome (BNFC).
	Zonisamide	At the time of publication, zonisamide did not have UK marketing authorisation for use in children younger than 18 years of age owing to insufficient data on safety and efficacy (SPC).
Tonic-atonic seizures	**Lamotrigine**	At the time of publication, lamotrigine did not have UK marketing authorisation for use in tonic-atonic seizures. It had authorisation for monotherapy and adjunctive treatment of focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome (BNFC).

	Topiramate	At the time of publication, topiramate did not have UK marketing authorisation for use in tonic-atonic seizures. It had authorisation for monotherapy and adjunctive treatment of focal seizures, GTC seizures and adjunctive treatment for seizures associated with Lennox–Gastaut syndrome (BNFC).
Infantile spasms	**ACTH (tetracosactide)**	At the time of publication, ACTH (tetracosactide) did not have UK marketing authorisation for infantile spasms. Depot ampoules are not recommended in infants and children younger than 3 years owing to the presence of benzyl alcohol in the formulation (SPC).
Lennox–Gastaut syndrome	**Felbamate**	At the time of publication, felbamate did not have UK marketing authorisation. There was no SPC available.
Dravet syndrome	**Topiramate**	At the time of publication, topiramate did not have UK marketing authorisation for use in Dravet syndrome but did have authorisation for generalised tonic–clonic seizures, focal seizures and seizures associated with Lennox–Gastaut syndrome (BNF).
BECTS/Panayiotopoulos syndrome and late-onset childhood occipital epilepsy (Gastaut type)	**Carbamazepine**	At the time of publication, carbamazepine did not have UK marketing authorisation for BECTS/Panayiotopoulos syndrome and late-onset childhood occipital epilepsy (Gastaut type) but had authorisation for focal and generalised tonic–clonic seizures (BNF).
	Lamotrigine	At the time of publication, lamotrigine did not have UK marketing authorisation for BECTS/Panayiotopoulos syndrome and late-onset childhood occipital epilepsy (Gastaut type) but had authorisation for focal and primary and generalised tonic–clonic seizures, seizures associated with Lennox–Gastaut syndrome and

		typical absence seizures (BNF).
	Oxcarbazepine	At the time of publication, oxcarbazepine did not have UK marketing authorisation for BECTS/Panayiotopoulos syndrome and late-onset childhood occipital epilepsy (Gastaut type) but had authorisation for focal seizures with or without generalised tonic–clonic seizures (BNF).
	Levetiracetam	At the time of publication, levetiracetam did not have UK marketing authorisation for BECTS/Panayiotopoulos syndrome and late-onset childhood occipital epilepsy (Gastaut type) but had authorisation for monotherapy and adjunctive treatment of focal seizures with or without secondary generalisation and adjunctive therapy for myoclonic and GTC seizures (BNFC).
IGE	**Clobazam**	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). This was because of insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
	Lamotrigine	At the time of publication, lamotrigine did not have UK marketing authorisation for use in IGE. It had authorisation for monotherapy and adjunctive treatment of focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome and monotherapy treatment of absence seizures in children (BNF).
	Levetiracetam	At the time of publication, levetiracetam did not have UK marketing authorisation for IGE but had authorisation for monotherapy and adjunctive treatment of focal seizures with or

		without secondary generalisation and adjunctive therapy for myoclonic and GTC seizures (BNF).
	Topiramate	At the time of publication, topiramate did not have UK marketing authorisation for use in IGE but had authorisation for focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome(BNF).
	Zonisamide	At the time of publication, zonisamide did not have UK marketing authorisation for use in IGE but had authorisation for adjunctive therapy for adult patients with partial seizures, with or without secondary generalisation (BNF).
Juvenile myoclonic epilepsy	**Clobazam**	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). This was because of insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
	Lamotrigine	At the time of publication, lamotrigine did not have UK marketing authorisation for use in juvenile myoclonic epilepsy (BNF) but had authorisation for monotherapy and adjunctive treatment of focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome and monotherapy treatment of absence seizures in children (BNF).
	Levetiracetam	At the time of publication, levetiracetam did not have UK marketing authorisation for monotherapy use in JME but had authorisation for monotherapy and adjunctive treatment of focal seizures with or without secondary generalisation and adjunctive therapy for myoclonic and GTC seizures (BNF).

	Topiramate	At the time of publication, topiramate did not have UK marketing authorisation for use in juvenile myoclonic epilepsy (BNF) but had authorisation for focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome (BNF).
	Zonisamide	At the time of publication, zonisamide did not have UK marketing authorisation for use in juvenile myoclonic epilepsy but had authorisation for adjunctive therapy for adult patients with partial seizures, with or without secondary generalisation. (BNF)
Absence syndromes	**Clobazam**	At the time of publication, clobazam did not have UK marketing authorisation for use in children younger than 3 years (BNFC). This was because of insufficient experience of the use of this drug in children younger than 3 years to enable any dosage recommendation to be made (SPC).
	Lamotrigine	At the time of publication, lamotrigine had UK marketing authorisation for monotherapy of typical absence seizures for those aged 2–12 years only. There was not authorisation outside of this age range (BNF).
	Levetiracetam	At the time of publication, levetiracetam did not have UK marketing authorisation for use in absence syndromes but had authorisation for monotherapy and adjunctive treatment of focal seizures with or without secondary generalisation and adjunctive therapy for myoclonic and GTC seizures (BNF).
	Topiramate	At the time of publication, topiramate did not have UK marketing authorisation for use in absence syndromes but had authorisation for focal seizures, GTC seizures and seizures associated with Lennox–Gastaut syndrome (BNF).

	Zonisamide	At the time of publication, zonisamide did not have UK marketing authorisation for use in absence syndromes but had authorisation for adjunctive therapy in the treatment of adult patients with partial seizures, with or without secondary generalisation (BNF).
Status epilepticus	**Propofol**	At the time of publication, propofol did not have UK marketing authorisation for status epilepticus but had authorisation for other conditions. Diprivan 2%, Propofol-Lipuro 2%, and Propoven 2% were not licensed for use in children younger than 3 years; Diprofusor TCI ('target controlled infusion') system was not licensed for use in children (BNFC).
	Thiopental sodium	At the time of publication, thiopental sodium did not have UK marketing authorisation for status epilepticus (only if other measures fail, see section 4.8.2 in BNF), by slow intravenous injection (BNF). It is authorised for convulsive states (75 mg to 125 mg or 3 ml to 5 ml of a 2.5% intravenous infusion) (SPC).
	Midazolam	At the time of publication, midazolam buccal liquid and injection did not have UK marketing authorisation for children with status epilepticus (BNF, BNFC).
	Diazepam	At the time of publication, diazepam did not have UK marketing authorisation for Rectubes and Stesolid Rectal Tubes or for use in children younger than 1 year (BNFC).

BECTS, benign epilepsy with centrotemporal spikes; BNF, British national formulary; BNFC, British national formulary for children; GTC, generalised tonic–clonic; SPC, summary of product characteristics.

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