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APPENDIX J

The key clinical questions and search strategies

Background link between the scope and questions

Questions listed have been developed in relation to the clinical areas covered in the NICE The Epilepsies Update guideline scope. Each question has been written to cover a specific dimension of an area in the scope. The questions have been developed by the NCGC technical team in consultation with the clinical advisor who has provided guidance on wording and clinical relevance of the specific questions.

The questions are structured according to the PICO format, i.e. they consist of the **population, intervention(s), comparison(s), and outcome(s)** of interest to the guideline developers. The purpose of formatting questions in this style is so that structured literature searches of relevant electronic databases (e.g. Medline, Embase, CINAHL) can be developed by the NCGC-ACC information scientists in order to identify relevant research studies.

Each question is essentially a topic for an individual systematic review conducted by the NCGC-ACC during the development phase of the guideline. Questions shaded in grey are to be combined and those in light blue are confirmed.

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<i>Clinical Question</i>	<i>Proposed Population</i>	<i>Proposed Intervention</i>	<i>Proposed Comparator</i>	<i>Proposed Outcome</i>	<i>Notes</i>
How effective and cost-effective are anti-epileptic drugs for partial with/without secondary generalisation	Adults and children with partial epilepsy with or without secondary generalisation seizures	Pregabalin	Placebo Carbamazepine Sodium valproate	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events (10% or above). • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<i>To report add-on therapy and monotherapy separately.</i>
		Zonisamide	Placebo Carbamazepine Sodium valproate		
		Lacosamide	Placebo Carbamazepine Sodium valproate		
		Lamotrigine	Placebo Carbamazepine Sodium valproate Gabapentin Levetiracetam Topiramate Phenytoin		

			Tiagabine Vigabatrin		
		Gabapentin	Placebo Carbamazepine Topiramate Oxcarbazepine Vigabatrin		
		Oxcarbazepine	Placebo Carbamazepine Sodium valproate Phenytoin topiramate		
		Tiagabine	Placebo Carbamazepine Phenytoin		
		Levetiracetam	Placebo Carbamazepine Sodium valproate		
		Topiramate	Placebo Carbamazepine Sodium valproate		
		Vigabatrin	Placebo Carbamazepine Sodium valproate		
		Phenytoin	Placebo Carbamazepine Sodium valproate Phenobarbitone		

			Primidone Clobazam		
		Phenobarbitone	Placebo Carbamazepine Sodium valproate Primidone		
		Felbamate	Placebo Carbamazepine Sodium valproate		
		Clobazam	Placebo Carbamazepine Sodium valproate		
		Clonazepam	Placebo Carbamazepine Sodium valproate		
		Acetazolamide	Placebo Carbamazepine Sodium valproate		
		Primidone	Placebo Sodium valproate		
		Sodium valproate	Placebo Carbamazepine		
		Sulthiame	Placebo Sodium Valproate Carbamazepine		

		Carbamazepine	Placebo		
How effective and cost-effective are anti-epileptic drugs for (primary) generalised tonic-clonic seizures	Adults and children with generalised tonic-clonic seizures	Lamotrigine	Placebo Carbamazepine Sodium valproate Phenytoin Topiramate Levetiracetam	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	To report add-on therapy and monotherapy separately.
		Levetiracetam	Placebo Carbamazepine Sodium valproate Phenytoin topiramate		
		Topiramate	Placebo Carbamazepine Sodium valproate		
		Oxcarbazepine	Placebo Carbamazepine Sodium valproate Phenytoin		
		Phenytoin	Placebo Carbamazepine Sodium valproate Phenobarbitone Primidone		
		Clobazam	Placebo Carbamazepine Sodium valproate		
		Clonazepam	Placebo		

			Carbamazepine Sodium valproate		
		Phenobarbitone	Placebo Carbamazepine Sodium valproate Primidone		
		Primidone	Placebo Carbamazepine Sodium valproate		
		Acetazolamide	Placebo Carbamazepine Sodium valproate		
		Sodium valproate	Placebo Carbamazepine		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Carbamazepine	Placebo		
How effective and cost-effective are anti-epileptic					

<p>drugs for Idiopathic Generalised Epilepsy?</p>					
<p>How effective and cost-effective are anti-epileptic drugs for absence seizures</p>	<p>Adults and children with absence seizures</p>	<p>Lamotrigine</p>	<p>Placebo Sodium valproate Topiramate Levetiracetam Ethosuximide Clobazam Clonazepam</p>	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>To report add-on therapy and monotherapy separately.</i></p>
		<p>Topiramate</p>	<p>Placebo Sodium valproate Levetiracetam Ethosuximide Clobazam Clonazepam</p>		
		<p>Levetiracetam</p>	<p>Sodium valproate Placebo</p>		
		<p>Ethosuximide</p>	<p>Placebo Sodium valproate Clobazam Clonazepam</p>		
		<p>Clobazam</p>	<p>Placebo Clonazepam Sodium valproate</p>		
		<p>Clonazepam</p>	<p>Placebo Sodium valproate</p>		
		<p>Zonisamide</p>	<p>Placebo</p>		

			Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for myoclonic seizures	Adults and children with myoclonic seizures	Lamotrigine	Placebo Sodium valproate Levetiracetam Topiramate Clobazam Clonazepam Piracetam	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	To report add-on therapy and monotherapy separately.
		Levetiracetam	Placebo Sodium valproate Topiramate Clobazam Clonazepam Piracetam		
		Topiramate	Placebo Sodium valproate Clobazam Clonazepam Piracetam		
		Clobazam	Placebo Sodium valproate Clonazepam Piracetam		

		Clonazepam	Placebo Sodium valproate Piracetam		
		Piracetam	Placebo Sodium valproate		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for tonic seizures	Adults and children with tonic seizures	Lamotrigine	Placebo Sodium valproate Levetiracetam Topiramate Clobazam Clonazepam Phenobarbitone Phenytoin Primidone	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<i>To report add-on therapy and monotherapy separately.</i>
		Levetiracetam	Placebo Sodium valproate Topiramate Clobazam Clonazepam Phenobarbitone		

			Phenytoin Primidone		
		Topiramate	Placebo Sodium valproate Clobazam Clonazepam Phenobarbitone Phenytoin Primidone		
		Clobazam	Placebo Sodium valproate Clonazepam Phenobarbitone Phenytoin Primidone		
		Clonazepam	Placebo Sodium valproate Phenobarbitone Phenytoin Primidone		
		Phenobarbitone	Placebo Sodium valproate Phenytoin Primidone		
		Phenytoin	Placebo Sodium valproate Primidone		
		Sodium valproate	Placebo Primidone		

		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Rufinamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Primidone	Placebo		
How effective and cost-effective are anti-epileptic drugs for atonic seizures	Adults and children with atonic seizures	Lamotrigine	Placebo Sodium valproate Levetiracetam Clobazam Clonazepam Topiramate	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive 	<i>To report add-on therapy and monotherapy separately.</i>
		Topiramate	Placebo Sodium valproate Levetiracetam Clobazam Clonazepam		

		Levetiracetam	Placebo Sodium valproate Clobazam Clonazepam	effects. <ul style="list-style-type: none"> Any outcomes relating to quality of life. 	
		Clobazam	Placebo Sodium valproate Clonazepam		
		Clonazepam	Placebo Topiramate Acetazolamide		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Rufinamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Sodium valproate	Placebo		
How effective	Children with	Lamotrigine	Placebo	<ul style="list-style-type: none"> The proportion of seizure-free 	

and cost-effective are anti-epileptic drugs for Childhood absence epilepsy	childhood absence epilepsy		Sodium valproate Ethosuximide Levetiracetam Topiramate	participants. <ul style="list-style-type: none"> • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<i>To report add-on therapy and monotherapy separately.</i> From HTAs.
		Levetiracetam	Placebo Sodium valproate Topiramate Ethosuximide Sodium valproate		
		Topiramate	Placebo Sodium valproate Ethosuximide		
		Ethosuximide	Placebo Sodium valproate		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Clobazam	Placebo Sodium valproate Clonazepam		
		Clonazepam	Placebo Topiramate		

			Acetazolamide		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for juvenile absence epilepsy	Children and adults with juvenile absence epilepsy	Lamotrigine	Placebo Sodium valproate Levetiracetam Topiramate Ethosuximide	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	To report add-on therapy and monotherapy separately.
		Levetiracetam	Placebo Sodium valproate Topiramate Ethosuximide		
		Topiramate	Placebo Sodium valproate Ethosuximide		
		Sodium valproate	Placebo Ethosuximide		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Clobazam	Placebo Sodium valproate Clonazepam		

		Clonazepam	Placebo Topiramate Acetazolamide		
		Ethosuximide	Placebo		
How effective and cost-effective are anti-epileptic drugs for Juvenile myoclonic epilepsy (JME)	Children and adults with juvenile myoclonic epilepsy	Lamotrigine	Placebo Sodium valproate Levetiracetam Topiramate Clobazam Clonazepam	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	To report add-on therapy and monotherapy separately.
		Levetiracetam	Placebo Sodium valproate Topiramate Clobazam Clonazepam		
		Topiramate	Sodium valproate Clobazam Clonazepam		
		Clobazam	Placebo Sodium valproate Clonazepam		
		Clonazepam	Placebo Sodium valproate		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate		

			Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for Infantile spasms	Children with infantile spasms	Nitrazepam	Placebo Sulthiame Pyridoxine ACTH Hydrocortisone Prednisolone Prednisone Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	To report add-on therapy and monotherapy separately.
		Pyridoxine	Placebo ACTH Hydrocortisone Prednisolone Prednisone Vigabatrin Topiramate Clobazam Clonazepam		
			Placebo Hydrocortisone Prednisolone Prednisone		

			Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate		
		Hydrocortisone	Placebo Prednisolone Prednisone Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate		
		Prednisolone	Placebo Prednisone Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate		
		Prednisone	Placebo Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate		
		Vigabatrin	Placebo Topiramate Clobazam Clonazepam Sodium valproate		

		Topiramate	Placebo Clobazam Clonazepam Sodium valproate		
		Clobazam	Placebo Clonazepam Sodium valproate		
		Clonazepam	Placebo Sodium valproate		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for Benign rolandic epilepsy/benign epilepsy with centrotemporal	Individuals with BECTS	Lamotrigine	Placebo Carbamazepine Sodium valproate Gabapentin Levetiracetam Topiramate Oxcarbazepine Levetiracetam Sulthiame	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated 	<i>To report add-on therapy and monotherapy separately.</i>

spikes (BECTS)				treatment (retention time). <ul style="list-style-type: none"> • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life.
	Levetiracetam	Placebo Carbamazepine Sodium valproate Gabapentin Topiramate Oxcarbazepine Sulthiame		
	Topiramate	Placebo Carbamazepine Sodium valproate Gabapentin Oxcarbazepine Sulthiame		
	Gabapentin	Placebo Carbamazepine Sodium valproate Oxcarbazepine Sulthiame		
	Oxcarbazepine	Placebo Sodium valproate Sulthiame		
	Sulthiame	Placebo Carbamazepine Sodium valproate		
	Sodium valproate	Placebo Carbamazepine		
	Carbamazepine	Placebo		

<p>How effective and cost-effective are anti-epileptic drugs for Benign epilepsy with occipital paroxysms</p>	<p>Adults and children with benign epilepsy with occipital paroxysms</p>	<p>Lamotrigine</p>	<p>Placebo Carbamazepine Sodium valproate Oxcarbazepine Levetiracetam Topiramate Levetiracetam Topiramate</p>	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>To report add-on therapy and monotherapy separately.</i></p>
<p>Oxcarbazepine</p>	<p>Placebo Carbamazepine Sodium valproate Levetiracetam Topiramate</p>				
<p>Levetiracetam</p>	<p>Placebo Carbamazepine Sodium valproate Topiramate</p>				
<p>Topiramate</p>	<p>Placebo Carbamazepine Sodium valproate</p>				
<p>Sodium valproate</p>	<p>Placebo Carbamazepine</p>				
<p>Carbamazepine</p>	<p>Placebo</p>				
<p>How effective and cost-effective are anti-epileptic drugs for Severe</p>	<p>individuals with SMEI</p>	<p>Stiripentol</p>	<p>Placebo Sodium valproate Levetiracetam Topiramate Clobazam</p>	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure 	<p><i>To report add-on therapy and monotherapy</i></p>

myoclonic epilepsy of infancy (SMEI)			Clonazepam Phenobarbitone	frequency (i.e. responders) <ul style="list-style-type: none"> • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	separately. From HTAs.
		Levetiracetam	Placebo Sodium valproate Topiramate Clobazam Clonazepam Phenobarbitone		
		Topiramate	Placebo Sodium valproate Clobazam Clonazepam Phenobarbitone		
		Clobazam	Placebo Sodium valproate Clonazepam Phenobarbitone		
		Clonazepam	Placebo Sodium valproate Phenobarbitone		
		Phenobarbitone	Placebo Sodium valproate		
		Sodium valproate	Placebo		
	How effective and cost-effective are anti-epileptic	Adults and children with CSWS	ACTH		

drugs for Continuous spike wave of slow sleep (CSWS)			Lamotrigine Topiramate Levetiracetam Ethosuximide Clobazam Clonazepam Sodium valproate	<p>least a 50% reduction in seizure frequency (i.e. responders)</p> <ul style="list-style-type: none"> • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>monotherapy separately.</i></p> <p>From HTAs.</p>
		Hydrocortisone	Placebo Prednisolone Prednisone Lamotrigine Topiramate Levetiracetam Ethosuximide Clobazam Clonazepam Sodium valproate		
		Prednisolone	Placebo Prednisone Lamotrigine Topiramate Levetiracetam Ethosuximide Clobazam Clonazepam Sodium valproate		
		Prednisone	Placebo Prednisone Lamotrigine Topiramate Levetiracetam Ethosuximide		

			Clobazam Clonazepam Sodium valproate		
		Lamotrigine	Placebo Topiramate Levetiracetam Ethosuximide Clobazam Clonazepam Sodium valproate		
		Topiramate	Placebo Levetiracetam Ethosuximide Clobazam Clonazepam Sodium valproate		
		Levetiracetam	Placebo Ethosuximide Clobazam Clonazepam Sodium valproate		
		Ethosuximide	Placebo Clobazam Clonazepam Sodium valproate		
		Clobazam	Placebo Clonazepam Sodium valproate		
		Clonazepam	Placebo		

			Sodium valproate		
		Sulthiame	Placebo Pyridoxine ACTH Hydrocortisone Prednisolone Prednisone Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for Lennox-Gastaut syndrome	Adults and children with Lennox-Gastaut syndrome	Rufinamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>To report add-on therapy and monotherapy separately.</i></p> <p>From HTAs.</p>
		Lamotrigine	Placebo Sodium valproate Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		

		Topiramate	Placebo Sodium valproate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Levetiracetam	Placebo Sodium valproate Felbamate Ethosuximide Clobazam Clonazepam		
		Felbamate	Placebo Sodium valproate Clobazam Clonazepam Ethosuximide		
		Ethosuximide	Placebo Sodium valproate Clobazam Clonazepam		
		Clobazam	Placebo Sodium valproate Clonazepam		
		Clonazepam	Placebo Sodium valproate		
		Sodium valproate	Placebo		

How effective and cost-effective are anti-epileptic drugs for Landau Kleffner Syndrome (LKS)	Adults and children with Landau Kleffner Syndrome	ACTH	Placebo Sodium valproate Prednisolone Lamotrigine Topiramate Levetiracetam Sulthiame	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>To report add-on therapy and monotherapy separately.</i></p> <p>From HTAs.</p>
		Prednisolone	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Sulthiame		
		Topiramate	Placebo Sodium valproate Lamotrigine Levetiracetam Sulthiame		
		Clobazam	Placebo Sodium valproate Clonazepam		
		Hydrocortisone	Placebo Prednisolone Prednisone Vigabatrin Topiramate Clobazam Clonazepam Sodium valproate		
		Lamotrigine	Placebo		

			Sodium valproate Levetiracetam Sulthiame		
		Levetiracetam	Placebo Sodium valproate Sulthiame		
		Sulthiame	Placebo Sodium valproate		
		Prednisone	Placebo ACTH Prednisolone Hydrocortisone		
		Sodium valproate	Placebo		
How effective and cost-effective are anti-epileptic drugs for Myoclonic astatic epilepsy (MAE)	Adults and children with MAE	Topiramate	Placebo Sodium valproate Lamotrigine Levetiracetam Ethosuximide Clobazam Clonazepam	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>To report add-on therapy and monotherapy separately.</i></p> <p>From Guideline.</p>
		Lamotrigine	Placebo Sodium valproate Levetiracetam Clobazam Clonazepam		
		Levetiracetam	Placebo Sodium valproate		

			Ethosuximide Clobazam Clonazepam		
		Ethosuximide	Placebo Sodium valproate Clobazam Clonazepam		
		Clobazam	Placebo Sodium valproate Clonazepam		
		Clonazepam	Placebo Sodium valproate		
		Zonisamide	Placebo Sodium valproate Lamotrigine Topiramate Levetiracetam Felbamate Ethosuximide Clobazam Clonazepam		
		Sodium valproate	Placebo		
Which AEDs are clinically effective and cost-effective for people with Convulsive status epilepticus?	Adults and children with status epilepticus.	Lorazepam	Placebo Clonazepam Diazepam Midazolam Paraldehyde	<ul style="list-style-type: none"> • Percentage of those whose seizure was stopped. • Duration of time to cessation of seizure. • Incidence of adverse events. 	<i>To report add-on therapy and monotherapy separately.</i>
		Diazepam	Placebo Midazolam		

			Clonazepam Paraldehyde Phenytoin		
		Midazolam	Placebo Clonazepam Propofol Paraldehyde		
		Clonazepam	Placebo Paraldehyde		
		Paraldehyde	Placebo		
		Phenytoin	Placebo Fosphenytoin Phenobarbitone Sodium valproate		
		Fosphenytoin	Placebo Phenobarbitone Sodium valproate		
		Phenobarbitone	Placebo Sodium valproate		
		Propofol	Placebo Pentobarbital		
		Thiopental	Placebo		

		Isoflurane	Placebo		
		Sodium Valproate	Placebo		
		Levetiracetam	Placebo		
		Pentobarbital	Placebo		
		Lidocaine			
Which AEDs are clinically effective and cost-effective for people with Non-Convulsive status epilepticus and Acute Repetitive Seizures ?	Adults and children with status epilepticus	Lorazepam	Placebo Clonazepam Diazepam Midazolam Paraldehyde		
		Diazepam	Placebo Midazolam Clonazepam Paraldehyde		
		Clobazam	Placebo Sodium Valproate Steroids Levetiracetam		
		Clonazepam	Placebo Sodium Valproate Steroids Levetiracetam		
		ACTH	Placebo		

		Prednisolone	Placebo		
		Levetiracetam	Placebo		
		Sodium valproate	Placebo Levetiracetam		
Which AEDs are clinically effective, cost-effective and safest for use in pregnancy?	Pregnant women with partial or generalised epilepsy. Women currently breast-feeding.	Pregabalin	Placebo Other AEDs	<ul style="list-style-type: none"> • Proportion of children born with major malformation. • Proportion of children born with minor malformation. • Miscarriage • Pharmacokinetics 	To report add-on therapy and monotherapy separately.
		Zonisamide			
		Lacosamide			
		Lamotrigine			
		Gabapentin			
		Oxcarbazepine			
		Tiagabine			
		Levetiracetam			

		Topiramate			
		Vigabatrin			
		Phenytoin			
		Phenobarbitone			
		Clonazepam			
		Clobazam			
		Felbamate			
		Acetazolamide			
		Primidone			
		Sodium valproate			

		Carbamazepine			
Which AEDs are the most tolerable for older people	People aged 65 years or over	Pregabalin	Placebo Other AEDs	<ul style="list-style-type: none"> • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<i>To report add-on therapy and monotherapy separately.</i>
		Zonisamide			
		Lacosamide			
		Lamotrigine			
		Gabapentin			
		Oxcarbazepine			
		Tiagabine			
		Levetiracetam			
		Topiramate			
		Vigabatrin			

		Phenytoin			
		Phenobarbitone			
		Clobazam			
		Clonazepam			
		Felbamate			
		Acetazolamide			
		Primidone			
		Sodium valproate			
		Carbamazepine			
Which AEDs are most tolerable	Adults and children with	Pregabalin		<ul style="list-style-type: none"> • Incidence of adverse events. 	<i>To report add-on</i>

for people with learning disabilities?	learning disabilities			<ul style="list-style-type: none"> • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	<p><i>therapy and monotherapy separately.</i></p>
		Zonisamide			
		Lacosamide			
		Lamotrigine			
		Gabapentin			
		Oxcarbazepine			
		Tiagabine			
		Levetiracetam			
		Topiramate			
		Vigabatrin			
Phenytoin					

		Phenobarbitone			
		Clobazam			
		Clonazepam			
		Felbamate			
		Acetazolamide			
		Primidone			
		Sodium valproate			
		Carbamazepine			
What is the incidence of side effects for AEDs?	Adults and children with any of the epilepsies	Stiripentol		<ul style="list-style-type: none"> • Drowsiness • Blood parameters 	<i>To report add-on therapy and monotherapy separately.</i>
		Lamotrigine		<ul style="list-style-type: none"> • Rash • Lack of sleep 	
		Levetiracetam		<ul style="list-style-type: none"> • Behaviour • Psychosis 	

				To report RCT data on side-effects..
		Tiagabine	<ul style="list-style-type: none"> • Induced nonconvulsive status 	
		Topiramate	<ul style="list-style-type: none"> • Slowness • Impairment of language • Weight loss • hyperthermia 	
		Vigabatrin	<ul style="list-style-type: none"> • Visual field defect • Aggravation of seizures • Behaviour 	
		Gabapentin	<ul style="list-style-type: none"> • Weight gain • 	
		Ethosuximide	<ul style="list-style-type: none"> • Nausea • Headache 	
		Felbamate	<ul style="list-style-type: none"> • Aplastic anaemia • Liver failure 	
		Clobazam	<ul style="list-style-type: none"> • Drowsiness 	
		Phenobarbitone	<ul style="list-style-type: none"> • Slowed learning 	
		Phenytoin	<ul style="list-style-type: none"> • Rash • Cosmetic side effects 	
		Sodium valproate	<ul style="list-style-type: none"> • Weigh gain • Hair loss • Liver toxicity 	

				<ul style="list-style-type: none"> • Menstrual irregularities • pancreatitis 	
		Carbamazepine		<ul style="list-style-type: none"> • Aplastic anaemia • rash 	
		Oxcarbazepine		<ul style="list-style-type: none"> • Headache • Low sodium • 	
		Ketogenic diet		<ul style="list-style-type: none"> • Renal stones • Change in cholesterol level • Cognitive impairment • Development 	
		General		Bone changes <ul style="list-style-type: none"> • Behaviour change • Seizure aggravation • Suicidality 	
What is the clinical effectiveness and cost-effectiveness of a ketogenic diet?	Children with epilepsy	Ketogenic diet	No change in diet No diet	<ul style="list-style-type: none"> • The proportion of seizure-free participants. • Proportion of participants experiencing at least a 50% reduction in seizure frequency (i.e. responders) • The proportion of participants having treatment withdrawn. • Time to exit/withdrawal of allocated treatment (retention time). • Time to first seizure (post randomisation). • Incidence of adverse events. • Any outcomes relating to cognitive effects. • Any outcomes relating to quality of life. 	

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2
3

1 **Literature search strategies**

2
3 Search strategies used for the Epilepsy guideline are outlined below and were run as per the NICE Guidelines Manual 2009
4 http://www.nice.org.uk/media/5F2/44/The_guidelines_manual_2009_-_All_chapters.pdf.
5

6 Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID), the Cochrane Library (Wiley Interscience) and Cinahl (EBSCO). Usually, searches
7 were constructed in the following way:

- 8 - A PICO format was used for **intervention** searches where population (P) terms were combined with Intervention (I) and sometimes Comparison (C)
9 terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search
10 Filters were also added to the search where appropriate.

11
12 Searches for the **health economic reviews** were run in Medline (Ovid), Embase (Ovid), The NHS Economic Evaluations Database (NHS EED) and the Health
13 Economic Evaluation Database (HEED). Searches in NHS EED and HEED were constructed only using population terms. For Medline and Embase an economic
14 filter (instead of a study type filter) was added to the same clinical search strategy. *Amend this section of accordingly.*

15
16 All searches were run up to 3 June 2010 unless otherwise stated. Any studies indexed in any of the databases after this date were not included unless
17 specifically stated in the text.

18
19 The clinical and economic search strategies are presented below in the following order:
20

Section 1.1	- Population terms by database. The same searches were used for all questions and for both clinical and health economic searches.
Section 1.2	- Study filter terms by database. These include filters for epidemiological study designs, health economic studies, quality of life studies and patient views [delete as appropriate].
Section 1.3	- Searches run for specific questions with the intervention or exposure terms by database. Order as presented in guideline
1.3.1	<ul style="list-style-type: none"> • Drugs included in first version of guideline or covered by two recent health technology assessments
1.3.2.	<ul style="list-style-type: none"> • Drugs not included in first version of guideline or covered by two recent health technology assessments

1.3.3	• Drugs included with pregnancy
1.3.4.	•
1.3.5	•
1.3.6	•
Section 1.4	- Economic searches

1 **1.1 Population search strategies**

2 **Medline search terms**

1	exp Epilepsy/
2	(epilep\$ or continous spike wave of slow sleep or landau-kleffner syndrome or lennox-gastaut syndrome or infant\$ spasm\$).ti,ab.
3	(seizure\$ or convulsion\$).ti,ab.
4	or/1-3

3
4 **Embase search terms**

1	exp Epilepsy/ or Landau Kleffner Syndrome/ or Infantile Spasm/
2	(epilep\$ or continous spike wave of slow sleep or landau-kleffner syndrome or lennox-gastaut syndrome or infant\$ spasm\$).ti,ab.
3	(seizure\$ or convulsion\$).ti,ab.
4	or/1-3

5
6 **Cinahl search terms**

1	(MH "Epilepsy")
2	TI epilep* or AB epilep*
3	"landau-kleffner syndrome"
4	"lennox-gastaut syndrome"

5	"infant* spasm*"
6	"continous spike wave of slow sleep"
7	S1 or S2 or S3 or S4 or S5 or S6

1
2

Cochrane search terms – Wiley interface

#1	MeSH descriptor Epilepsy explode all trees
#2	(epilep* or continous spike wave of slow sleep or landau-kleffner syndrome or lennox-gastaut syndrome):ti,ab,kw
#3	(seizure* or convulsion*):ti,ab,kw
#4	(#1 OR #2 OR #3)

3
4

NHS Economic Evaluations Database – Centre for Reviews and Dissemination

#1	MeSH Epilepsy EXPLODE 1
#2	epilep* or seizure* or convulsion*
#3	#1 or #2

5
6

HEED (Health Economic Evaluations Database

#1	epilep* or seizure* or convulsion*
----	------------------------------------

7

8 **1.2 Study design search terms**

9 **1.2.1 Systematic review search terms**

10 **Medline search terms**

1	meta-analysis/
2	(metaanalys\$ or meta-analys\$ or meta analys\$).tw.
3	(systematic\$ adj3 (review\$ or overview\$)).tw.
4	(selection criteria or data extraction).ab. and review.pt.

5	(cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or bids or cancerlit).ab.
6	(reference list\$ or bibliograph\$ or hand search\$ or hand-search\$ or manual search\$ or relevant journals).ab.
7	or/1-6
8	(comment or letter or editorial).pt.
9	animal/ not human/
10	8 or 9
11	7 not 10

1
2

Embase search terms

1	meta-analysis/
2	(metaanalys\$ or meta-analys\$ or meta analys\$).tw.
3	(systematic\$ adj3 (review\$ or overview\$)).tw.
4	(selection criteria or data extraction).ab. and review.pt.
5	(cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or bids or cancerlit).ab.
6	(reference list\$ or bibliograph\$ or hand search\$ or hand-search\$ or manual search\$ or relevant journals).ab.
7	or/1-6
8	(letter or editorial).pt.
9	(exp animal/ or nonhuman/ or exp animal-experiment/) not exp human/
10	8 or 9
11	7 not 10

3

4 **1.2.2 Randomised controlled studies (RCTs) search terms**

5 **Medline search terms**

1	Randomized-Controlled-Trials/ or Random-Allocation/ or Double-Blind-Method/ or Single-Blind-Method/ or exp Clinical-Trials as topic/ or Cross-Over-Studies/ or Prospective-Studies/ or Placebos/
2	(Randomized-Controlled-Trial or Clinical-Trial or Controlled-Clinical-Trial).pt.
3	(((((((((clinical or control or controlled) adj (study or trial)) or (single or double or triple)) adj (blind\$3 or mask\$3)) or randomised or randomized or random\$) adj (assign\$ or allocat\$ or group or grouped or patients or study or trial or distribut\$)) or crossover) adj (design or study or trial)) or placebo or placebos).ti,ab.
4	((Case-Reports not Randomized-Controlled-Trial) or Letter or Historical-Article or Review-Of-Reported-Cases).pt.
5	Animal/ not Human/
6	(1 or 2 or 3) not (4 or 5)

1
2

Embase search terms

1	Clinical-Trial/ or Randomized-Controlled-Trial/ or Randomization/ or Single-Blind-Procedure/ or Double-Blind-Procedure/ or Crossover-Procedure/ or Prospective-Study/ or Placebo/
2	(((((((((clinical or control or controlled) adj (study or trial)) or (single or double or triple)) adj (blind\$3 or mask\$3)) or randomised or randomized or random\$) adj (assign\$ or allocat\$ or group or grouped or patients or study or trial or distribut\$)) or crossover) adj (design or study or trial)) or placebo or placebos).ti,ab.
3	Case-Study/ or Abstract-Report/ or Letter/ or (case adj report).tw.
4	(exp Animal/ or Nonhuman/ or exp Animal-Experiment/) not exp Human/
5	(1 or 2) not (3 or 4)

3
4

Cinahl search terms

1	((MH "Random Assignment") or (MH "Random Sample+") or (MH "Crossover Design") or (MH "Clinical Trials+") or (MH "Comparative Studies") or (MH "Control (Research)+") or (MH "Control Group") or (MH "Factorial Design") or (MH "Quasi-Experimental Studies+") or (MH "Placebos") or (MH "Meta Analysis") or (MH "Sample Size") or (MH "Research, Nursing") or (MH "Research Question") or (MH
---	--

	"Research Methodology+" or (MH "Evaluation Research+") or (MH "Concurrent Prospective Studies") or (MH "Prospective Studies") or (MH "Nursing Practice, Research-Based") or (MH "Solomon Four-Group Design") or (MH "One-Shot Case Study") or (MH "Pretest-Posttest Design+") or (MH "Static Group Comparison") or (MH "Study Design") or (MH "Clinical Research+") or (clinical nursing research or random* or cross?over or placebo* or control* or factorial or sham* or meta?analy* or systematic review* or blind* or mask* or trial*)
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1

2 **1.2.3 Observational studies search terms**

3 **Medline search terms**

1	exp cohort studies/ or epidemiologic methods/ or exp case-control studies/
2	cohort\$.tw.
3	(case\$ and control\$).tw.
4	(case\$ and series).tw.
5	or/1-4
6	Animal/ not Human/
7	5 not 6

4

5 **Embase search terms**

1	exp cohort analysis/ or exp longitudinal study/ or exp prospective study/ or exp follow up/ or exp case control study/ or exp case study/
2	cohort\$.tw.
3	(case\$ and control\$).tw.
4	(case\$ and series).tw.
5	or/1-4
6	(exp Animal/ or Nonhuman/ or exp Animal-Experiment/) not exp Human/
7	5 not 6

6

1 **1.2.4 Health economic search filter**

2 **Medline search terms**

1	exp "Costs and Cost Analysis"/
2	Economics/
3	Economics, Nursing/ or Economics, Medical/ or Economics, Hospital/ or Economics, Pharmaceutical/
4	exp "Fees and Charges"/
5	exp Budgets/
6	budget\$.tw.
7	cost\$.ti.
8	(cost\$ adj2 (effective\$ or utilit\$ or benefit\$ or minimi\$)).ab.
9	(economic\$ or pharmaco-economic\$ or pharmaco-economic\$).ti.
10	(price\$ or pricing\$).tw.
11	(financial or finance or finances or financed).tw.
12	(fee or fees).tw.
13	(value adj2 (money or monetary)).tw.
14	or/1-13

3
4 **Embase search terms**

1	exp economic aspect/
2	cost\$.ti.
3	(cost\$ adj2 (effective\$ or utilit\$ or benefit\$ or minimi\$)).ab.
4	(economic\$ or pharmaco-economic\$ or pharmaco-economic\$).ti.
5	(price\$ or pricing\$).ti.
6	(fee or fees).ti.
7	(financial or finance or finances or financed).tw.
8	(value adj2 (money or monetary)).tw.

9	or/1-8
---	--------

1

2 **1.2.5 Quality of life search filter**

3 **Medline search terms**

1	"Value of Life"/
2	quality adjusted life.tw.
3	(qaly\$ or qald\$ or qale\$ or qtime\$).tw.
4	disability adjusted life.tw.
5	daly\$.tw.
6	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
7	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
8	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
9	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
10	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
11	(euroqol or euro qol or eq5d or eq 5d).tw.
12	(hql or hqol or h qol or hrqol or hr qol).tw.
13	(hye or hyes).tw.
14	health\$ equivalent\$ year\$.tw.
15	(hui or hui1 or hui2 or hui3).tw.
16	health utilit\$.tw.
17	disutilit\$.tw.

18	rosser.tw.
19	(quality of wellbeing or quality of well being).tw.
20	qwb.tw.
21	willingness to pay.tw.
22	standard gamble\$.tw.
23	time trade off.tw.
24	time tradeoff.tw.
25	tto.tw.
26	or/1-25

1
2

Embase search terms

1	quality adjusted life.tw.
2	(qaly\$ or qald\$ or qale\$ or qtime\$).tw.
3	disability adjusted life.tw.
4	daly\$.tw.
5	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
6	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
7	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
8	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
9	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
10	(euroqol or euro qol or eq5d or eq 5d).tw.
11	(hql or hqol or h qol or hrqol or hr qol).tw.
12	(hye or hyes).tw.

13	health\$ equivalent\$ year\$.tw.
14	(hui or hui1 or hui2 or hui3).tw.
15	health utilit\$.tw.
16	disutilit\$.tw.
17	rosser.tw.
18	(quality of wellbeing or quality of well being).tw.
19	qwb.tw.
20	willingness to pay.tw.
21	standard gamble\$.tw.
22	time trade off.tw.
23	time tradeoff.tw.
24	tto.tw.
25	or/1-24

1

2 **1.2.6 Economic modelling search terms**

3 **Medline search terms**

1	exp models, economic/
2	models, theoretical/ or models, organizational/
3	economic model\$.tw.
4	markov chains/
5	markov\$.tw.
6	Monte Carlo Method/
7	monte carlo.tw.
8	exp Decision Theory/
9	(decision\$ adj2 (tree\$ or anlay\$ or model\$)).tw.
10	or/1-9

1

2

Embase search terms

1	exp Mathematical Model/
2	economic model\$.tw.
3	markov\$.tw.
4	Monte Carlo Method/
5	monte carlo.tw.
6	exp Decision Theory/
7	(decision\$ adj2 (tree\$ or anlay\$ or model\$)).tw.
8	or/1-8

3

4

1.2.7 Patient views search terms

5

1.2.8 Add or delete from above as applicable

6

7

1.3 Drug searches

8

The following questions were searched for as two main searches. One for drugs covered by the previous version of the guideline{Stokes, 2004 5197 /id} or two recent health technology assessments (HTAs){Wilby, 2005 4685 /id;Connock, 2006 5196 /id}, and the other for drugs not included in these publications. In the first search, the final date of searches was in 2003 for the previous guideline and 2002 for the HTA reports, consequently, the start date for searches in this guideline ran was 2002. The second search included all dates covered by the databases. The strategies are presented in the two sections immediately following the list of questions.

14

How effective and cost-effective are anti-epileptic drugs for:

16

- partial epilepsy with/without secondary generalisation

- 1 • (primary) generalised tonic-clonic seizures
- 2 • Idiopathic Generalised Epilepsy (IGE)
- 3 • absence seizures
- 4 • myoclonic seizures
- 5 • tonic seizures
- 6 • atonic seizures/
- 7 • childhood absence epilepsy?
- 8 • juvenile absence epilepsy
- 9 • Juvenile Myoclonic Epilepsy (JME)
- 10 • infantile spasms
- 11 • benign rolandic epilepsy/benign epilepsy with centrotemporal spikes (BECTS)
- 12 • benign epilepsy with occipital paroxysms
- 13 • Severe Myoclonic Epilepsy of Infancy (SMEI)
- 14 • Continuous Spike Wave of Slow Sleep (CSWS)
- 15 • Lennox-Gastaut syndrome
- 16 • Landau Kleffner Syndrome (LKS)
- 17 • Myoclonic Astatic Epilepsy (MAE)
- 18 • people with convulsive status epilepticus?
- 19 • people with non-convulsive status epilepticus and acute repetitive seizures?
- 20
- 21 Which anti-epileptic drugs are the most tolerable for older people?
- 22 Which anti-epileptic drugs are most tolerable for people with learning disabilities?
- 23 What is the incidence of side effects for anti-epileptic drugs?
- 24 What is the clinical effectiveness and cost-effectiveness of a ketogenic diet?
- 25

1 **1.3.1 Drugs included in previous guideline or Health Technology Assessment**

Population	Intervention / exposure	Comparison	Study filters used	Date parameters
Epilepsy	Drugs included in previous guideline	Each other or placebo	Systematic reviews, RCTs (Medline, Embase & Cinahl only) Health economics, quality of life, economic modelling (Medline and Embase only)	2002 to 03/06/10

2
3

Medline & Embase search terms

1	(Gabapentin or Neurontin or neurotonin or gbp or 1 aminomethyl cyclohexaneacetic acid or goe 3450 or go 3450 or ci 945).mp.
2	(Lamotrigine or Crisomet or Labileno or Lamictal or Lamiktal or 3 5-diamino-6-2 3-dichlorophenyl-as-triazine or dichlorophenyltriazinediyldiamine or BW 430C or bw 430 c or bw 430c78 or ltg).mp.
3	(Levetiracetam or Etiracetam or Keppra or lev or lvt or 1-1-carbanmoylpropyl-2-pyrrolidinone or alpha-ethyl-2-oxo-1-pyrrolidineacetamide or UCB 6474 or UCB-L059 or UCB-L060 or lo 59).mp.
4	(Oxcarbazepine or Timox or Trileptal or GP 47680 or oxc).mp.
5	(Tiagabine or Gabitril or R-4 4-bis 3-methyl-2-thienyl-3-butenyl-3-piperidinecarboxylic acid hydrochloride or N-4 4-di 3-methylthien-2-yl but-3-enyl nipecotic acid or NO 328 or NO 329 or "nnc 05 0328" or nnc 328 or "no 05 0328" or no 328 or no 329 or tiabex or tgb).mp.
6	(Topiramate or Epitomax or Topamax or topimax or 2 3-4 5-bis-O-1-

	methylethylidene-beta-D-fructopyranose sulfamate or McN 4853 or rwj 17021 or tpm).mp.
7	(Vigabatrin or Sabril or Sabrilex or gamma-Vinyl-GABA or 3 amino 5 carboxyhexene or 4 amino 4 ethenylbutyric acid or 4 amino 4 vinylbutyric acid or 4 amino 4 vinylbutanoic acid or 4 amino 4 aminobutyric acid or 4 amino 5 hexenoic acid or 4 aminohex 5 enoic acid or 4 vinylaminobutyric acid or 4 vinylgaba or gamma vinyl 4 aminobutyric acid or gamma vinyl gaba or gamma vinylgaba or gamma vinyl gamma aminobutyric acid or mdl 71754 or n vinyl 4 aminobutyric acid or n vinyl gaba or n vinyl gamma aminobutyric acid or rmi 71754 or rmi 71890 or sabril or sabrilex or gvg or vgb).mp.
8	or/1-7
9	(Acetazolamide or Acetadiazol or Acetazolam or Diacarb or Diamox or Diuramide or Defiltran or Edemox or Glauconox or Glaupax or Huma-Zolamide or Ak-Zol).mp.
10	(Clobazam or Frisium or Urbanyl or HR 376).mp.
11	(Carbamazepine or Amizepine or Carbazepin or Epitol or Finlepsin or Neurotol or Tegretol).mp.
12	(Clonazepam or Antelepsin or Rivotril).mp.
13	(Ethosuximide or Emeside or Ethosuccimid or Ethylmethylsuccimide or Ethymal or Etosuximida Faes or Petnidan or Pyknolepsinum or Suksilep or Suxilep or Zarontin).mp.
14	(Felbamate or Felbamyl or Felbatol or Taloxa or 2-phenyl-1 3-propanediol dicarbamate or ADD-03055 or W-554).mp.
15	(Phenobarbitone or Gardenal or Hysteps or Luminal or Phenemal or Phenobarbitone or Phenylbarbital or Phenylethylbarbituric Acid).mp.
16	(Phenytoin or Antisacer or Difenin or Dihydan or Dilantin or Diphenylhydantoin or Epamin or Epanutin or Fenitoin or Hydantol or 5 5-Diphenylhydantoin or Sodium Diphenylhydantoinate).mp.
17	(Piracetam or Avigilen or Axonyl or Cerebroforte or Cerepar N or Ciclofalina or Cuxabrain or Dinagen or Gabacet or Geram or Memo-Puren or Nootrop or Nootropil or Nootropyl or Normabrain or Piracebral or Piracetrop or Piracetam or Pyracetam or Pyramem or Sinapsan or UCB-6215 or 2-Pyrrolidone-N-Acetamide).mp.

18	(Primidone or Liskantin or Misodine or Mizodin or Mylepsinum or Mysoline or Primaclone or Resimatil or Sertan or Desoxyphenobarbital).mp.
19	(Valproic Acid or 2-Propylpentanoic Acid or Convulsofin or Depakene or Depakine or Depakote or Dipropyl Acetate or Divalproex or Divalproex Sodium or Ergenyl or Valproate or Vupral).mp.
20	(Sulthiame or Ospolot or sultiam).mp.
21	(Pentobarbitone or Pentobarbital or Diabutal or Etaminal or Ethaminal or Mebubarbital or Mebumal or Nembutal or Sagatal).mp.
22	(Propofol or Aquafol or Diprivan or Disoprivan or Disoprofol or Fresofol or Ivofol or Recofol or 2 6-Bis 1-methylethyl pheno or 2 6-Diisopropylphenol or ICI-35 or868 or ICI-35868).mp.
23	(Midazolam or Dormicum or Ro 21-3981 or versed).mp.
24	(Lorazepam or Ativan or Duralozam or Durazolam or Idalprem or Laubeel or Novo-Lorazem or Nu-Loraz or Orfidal Wyeth or Sedicepan or Sinestron or Somagerol or Temesta or Tolid or WY-4036 or Donix or lorazep von ct).mp.
25	Paraldehyde.mp.
26	Ketogenic diet\$.mp.
27	or/9-26
28	8 or 27

1
2

Cinahl search terms

S1	Gabapentin or Neurontin or neurotonin
S2	Lamotrigine or Crisomet or Labileno or Lamictal or Lamiktal
S3	levetiracetam or Etiracetam or Keppra
S4	Oxcarbazepine or Timox or Trileptal
S5	Tiagabine or Gabitril
S6	Topiramate or Epitomax or Topamax or topimax
S7	Vigabatrin or Sabril or Sabrilex
S8	Acetazolamide or Acetadiazol or Acetazolam or Diacarb or Diamox or Diuramide or

	Defiltran or Edemox or Glauconox or Glau-pax or Huma-Zolamide
S9	Clobazam or Frisium or Urbanyl
S10	Carbamazepine or Amizepine or Carbazepin or Epitol or Finlepsin or Neurotol or Tegretol
S11	Clonazepam or Antelepsin or Rivotril
S12	Ethosuximide or Emeside or Ethosuccimid or Ethylmethylsuccimide or Ethymal or Etosuximida Faes or Petnidan or Pyknolepsinum or Suksilep or Suxilep or Zarontin
S13	Felbamate or Felbamyl or Felbatol or Taloxa
S14	Phenobarbitone or Gardenal or Hysteps or Luminal or Phenemal or Phenobarbitone or Phenylbarbital or Phenylethylbarbituric Acid
S15	Phenytoin or Antisacer or Difenin or Dihydan or Dilantin or Diphenylhydantoin or Epamin or Epanutin or Fenitoin or Hydantol or Sodium Diphenylhydantoinate
S16	Piracetam or Avigilen or Axonyl or Cerebroforte or Cerepar N or Ciclofalina or Cuxabrain or Dinagen or Gabacet or Geram or Memo-Puren or Nootrop or Nootropil or Nootropyl or Normabrain or Piracebral or Piracetrop or Pirazetam or Pyracetam or Pyramem or Sinapsan or UCB-6215
S17	Primidone or Liskantin or Misodine or Mizodin or Mylepsinum or Mysoline or Primaclone or Resimatil or Sertan or Desoxyphenobarbital
S18	Valproic Acid or 2-Propylpentanoic Acid or Convulsofin or Depakene or Depakine or Depakote or Dipropyl Acetate or Divalproex or Divalproex Sodium or Ergenyl or Valproate or Vupral
S19	Sulthiame or Ospolot or sultiam
S20	pentobarbitone or pentobarbitonal or Diabutal or Etaminal or Ethaminal or Mebubarbital or Mebumal or Nembutal or Sagatal
S21	propofol or Aquafol or Diprivan or Disoprivan or Disoprofol or Fresofol or Ivofol or Recofol
S22	midazolam or Dormicum
S23	lorazepam or Ativan or Duralozam or Durazolam or Idalprem or Laubeel or Novo-Lorazem or Nu-Loraz or Orfidal Wyeth or Sedicepan or Sinestron or Somagerol or Temesta or Tolid or Temesta or WY-4036
S24	paraldehyde
S25	Ketogenic diet or ketogenic diets

S26	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25
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Cochrane search terms – Wiley interface

#1	(Gabapentin or Neurontin or neurotonin or gbp or 1 aminomethyl cyclohexaneacetic acid or goe 3450 or go 3450 or ci 945):ti,ab,kw
#2	(Lamotrigine or Crisomet or Labileno or Lamictal or Lamiktal or 3 5-diamino-6-2 3-dichlorophenyl-as-triazine or dichlorophenyltriazinediyldiamine or BW 430C or bw 430 c or bw 430c78 or ltg):ti,ab,kw
#3	(Levetiracetam or Etiracetam or Keppra or lev or lvt or 1 1 carbanmoylpropyl 2 pyrrolidinone or alpha-ethyl-2-oxo-1-pyrrolidineacetamide or UCB 6474 or UCB-L059 or UCB-L060 or lo 59):ti,ab,kw
#4	(Oxcarbazepine or Timox or Trileptal or GP 47680 or oxc):ti,ab,kw
#5	(Tiagabine or Gabitril or R-4 4-bis 3-methyl-2-thienyl-3-butenyl-3-piperidinecarboxylic acid hydrochloride or N-4 4-di 3-methylthien-2-yl but-3-enyl nipecotic acid or NO 328 or NO 329 or nnc 05 0328 or nnc 328 or no 05 0328 or no 328 or no 329 or tiabex or tgb):ti,ab,kw
#6	(Topiramate or Epitomax or Topamax or topimax or 2 3-4 5-bis-O-1-methylethylidene-beta-D-fructopyranose sulfamate or McN 4853 or rwj 17021 or tpm):ti,ab,kw
#7	(Vigabatrin or Sabril or Sabrilex or gamma-Vinyl-GABA or 3 amino 5 carboxyhexene or 4 amino 4 ethenylbutyric acid or 4 amino 4 vinylbutyric acid or 4 amino 4 vinylbutanoic acid or 4 amino 4 aminobutyric acid or 4 amino 5 hexenoic acid or 4 aminohex 5 enoic acid or 4 vinylaminobutyric acid or 4 vinylgaba or gamma vinyl 4 aminobutyric acid or gamma vinyl gaba or gamma vinylgaba or gamma vinyl gamma aminobutyric acid or mdl 71754 or n vinyl 4 aminobutyric acid or n vinyl gaba or n vinyl gamma aminobutyric acid or rmi 71754 or rmi 71890 or sabril or sabrilex or gvg or vgb):ti,ab,kw
#8	(Acetazolamide or Acetadiazol or Acetazolam or Diacarb or Diamox or Diuramide or Defiltran or Edemox or Glauconox or Glaupax or Huma-Zolamide or Ak-Zol):ti,ab,kw
#9	(Clobazam or Frisium or Urbanyl or HR 376):ti,ab,kw
#10	(Carbamazepine or Amizepine or Carbazepin or Epitol or Finlepsin or Neurotol or Tegretol):ti,ab,kw
#11	(Clonazepam or Anteplepsin or Rivotril):ti,ab,kw

#12	(Ethosuximide or Emeside or Ethosuccimid or Ethylmethylsuccimide or Ethymal or Etosuximida Faes or Petnidan or Pyknolepsinum or Suksilep or Suxilep or Zarontin):ti,ab,kw
#13	(Felbamate or Felbamyl or Felbatol or Taloxa or 2-phenyl-1 3-propanediol dicarbamate or ADD-03055 or W-554):ti,ab,kw
#14	(Phenobarbitone or Gardenal or Hysteps or Luminal or Phenemal or Phenobarbitone or Phenylbarbital or Phenylethylbarbituric Acid):ti,ab,kw
#15	(Phenytoin or Antisacer or Difenin or Dihydan or Dilantin or Diphenylhydantoin or Epamin or Epanutin or Fenitoin or Hydantol or 5 5-Diphenylhydantoin or Sodium Diphenylhydantoinate):ti,ab,kw
#16	(Piracetam or Avigilen or Axonyl or Cerebroforte or Cerepar N or Ciclofalina or Cuxabrain or Dinagen or Gabacet or Geram or Memo-Puren or Nootrop or Nootropil or Nootropyl or Normabrain or Piracebral or Piracetrop or Pirazetam or Pyracetam or Pyramem or Sinapsan or UCB-6215 or 2-Pyrrolidone-N-Acetamide):ti,ab,kw
#17	(Primidone or Liskantin or Misodine or Mizodin or Mylepsinum or Mysoline or Primaclone or Resimatil or Sertan or Desoxyphenobarbital):ti,ab,kw
#18	(Valproic Acid or 2-Propylpentanoic Acid or Convulsofin or Depakene or Depakine or Depakote or Dipropyl Acetate or Divalproex or Divalproex Sodium or Ergenyl or Valproate or Vupral):ti,ab,kw
#19	(Sulthiame or Ospolot or sultiam):ti,ab,kw
#20	(Pentobarbitone or Pentobarbital or Diabutal or Etaminal or Ethaminal or Mebubarbital or Mebumal or Nembutal or Sagatal):ti,ab,kw
#21	(Propofol or Aquafol or Diprivan or Disoprivan or Disoprofol or Fresofol or Ivofol or Recofol or 2 6-Bis 1-methylethyl pheno or 2 6-Diisopropylphenol or ICI-35 or868 or ICI-35868):ti,ab,kw
#22	(Midazolam or Dormicum or Ro 21-3981 or versed):ti,ab,kw
#23	(Lorazepam or Ativan or Duralozam or Durazolam or Idalprem or Laubeel or Novo-Lorazem or Nu-Loraz or Orfidal Wyeth or Sedicepan or Sinestron or Somagerol or Temesta or Tolid or WY-4036 or Donix or lorazep von ct):ti,ab,kw
#24	Paraldehyde:ti,ab,kw
#25	(Ketogenic diet*):ti,ab,kw
#26	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25

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2 **1.3.2 Drugs not covered by previous guideline or HTA report**

Population	Intervention / exposure	Comparison	Study filters used	Date parameters
Epilepsy	Drugs included in previous guideline	Each other or placebo	Systematic reviews, RCTs (Medline, Embase & Cinahl only) Health economics, quality of life, economic modelling (Medline and Embase only)	Start dates: Medline 1950, Embase 1980, Cinahl 1982 Searched up to: 03/06/10

3

4 **Medline & Embase search terms**

1	(pregabalin or Lyrica or 3 isobutyl GABA).mp.
2	(rufinamide or CGP 33101 or 1 2 6 difluorobenzyl 1H 1 2 3 triazole 4 carboxamide).mp.
3	(zonisamide or Zonegran or AD 810 o 1 2 benzisoxazole 3 methanesulfonamide or 3 sulfamoylmethyl 1 2 benzisoxazole).mp.
4	(lacosamide or N-benzyl-2-acetamido-3-methoxypropionamide or N-benzyl-AcMeOPrNH2).mp.
5	(stiripentol or D-306).mp.
6	(nitrazepam or Alodorm or Dormalon or Dormo-Puren or Eatan or Imadorm or imeson or Mogadon or Nitrazadon or Nitrazep or Nitrodiazepam or Novanox or Radedorm or Remnos or Serenade or Somnite).mp.
7	(prednisolone or Di-Adreson-F or Predate or Predonine).mp.

8	(hydrocortisone or Cortifair or Cortisol or Cortril or Epicortisol).mp.
9	(Prednisone or Cortan or Cortancyl or Cutason or Dacortin or Decortisyl or Dehydrocortisone or delta-Cortisone or Deltasone or Encorton or Encortone or Enkortolon or Kortancyl or Liquid Pred or Meticorten or Orasone or Panafcort or Panasol or Predni Tablinen or Prednidib or Predniment or Prednison acsis or Prednison Galen or Prednison Hexal or Pronisone or Rectodelt or Sone or Sterapred or Ultracorten or Winpred).mp.
10	adrenocorticotrophin.mp.
11	(fosphenytoin or Cerebyx or HMPDP or Prodilantin or ACC-9653 or 3-hydroxymethyl phenytoin disodium phosphate or 3 hydroxymethyl phenytoin phosphate ester).mp.
12	isoflurane.mp.
13	(thiopentone or bomathal or penthiobarbital or pentothal or pentothal sodico or sodipental or thionembumal or thionembutal or thiopentobarbital or thiopentone or tiobarbital braun or trapanal).mp.
14	(diazepam or 7-chloro-1 3-dihydro-1-methyl-5-phenyl-2h-1 4-benzodiazepin-2-one or apaurin or diazemuls or faustan or relanium or seduxen or sibazon or stesolid or valium).mp.
15	(eslicarbazepine acetate or S-licarbazepine or zebinix).mp.
16	or/1-16

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Cinahl search terms

S1	pregabalin or Lyrica
S2	rufinamide or CGP 33101 or 1 2 6 difluorobenzyl 1H 1 2 3 triazole 4 carboxamide
S3	zonisamide or Zonegran or AD 810 o 1 2 benzisoxazole 3 methanesulfonamide or 3 sulfamoylmethyl 1 2 benzisoxazole
S4	lacosamide or N-benzyl-2-acetamido-3-methoxypropionamide or N-benzyl-AcMeOPrNH2
S5	stiripentol or D-306
S6	nitrazepam or Alodorm or Dormalon or Dormo-Puren or Eatan or Imadorm or imeson or Mogadon or Nitrazadon or Nitrazep or Nitrodiazepam or Novanox or

	Radedorm or Remnos or Serenade or Somnite
S7	prednisolone or Di-Adreson-F or Predate or Predonine
S8	Prednisone or Cortan or Cortancyl or Cutason or Dacortin or Decortisyl or Dehydrocortisone or delta-Cortisone or Deltasone or Encorton or Encortone or Enkortolon or Kortancyl or Liquid Pred or Meticorten or Orasone or Panafcort or Panasol or Predni Tablinen or Prednidib or Predniment or Prednison acsis or Prednison Galen or Prednison Hexal or Pronisone or Rectodelt or Sone or Sterapred or Ultracorten or Winpred
S9	hydrocortisone or Cortifair or Cortisol or Cortril or Epicortisol
S10	adrenocorticotrophin
S11	fosphenytoin or Cerebyx or HMPDP or Prodilantin or ACC-9653 or 3- hydroxymethyl phenytoin disodium phosphate or 3 hydroxymethyl phenytoin phosphate ester
S12	thiopentone or bomathal or penthiobarbital or pentothal or pentothal sodico or sodipental or thiomebumal or thionembatal or thiopentobarbital or thiopentone or tiobarbital braun or trapanal
S13	diazepam or 7-chloro-1 3-dihydro-1-methyl-5-phenyl-2h-1 4-benzodiazepin-2-one or apaurin or diazemuls or faustan or relanium or seduxen or sibazon or stesolid or valium
S14	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13

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Cochrane search terms – Wiley interface

#1	pregabalin or Lyrica
#2	(rufinamide or CGP 33101 or 1 2 6 difluorobenzyl 1H 1 2 3 triazole 4 carboxamide):ti,ab,kw
#3	(zonisamide or Zonegran or AD 810 o 1 2 benzisoxazole 3 methanesulfonamide or 3 sulfamoylmethyl 1 2 benzisoxazole):ti,ab,kw
#4	(lacosamide or N-benzyl-2-acetamido-3-methoxypropionamide or N-benzyl-AcMeOPrNH2):ti,ab,kw
#5	(stiripentol or D-306):ti,ab,kw
#6	(nitrazepam or Alodorm or Dormalon or Dormo-Puren or Eatan or Imadorm or imeson or Mogadon or Nitrazadon or Nitrazep or Nitrodiazepam or Novanox or Radedorm or Remnos or Serenade or Somnite):ti,ab,kw

#7	(prednisolone or Di-Adreson-F or Predate or Predonine):ti,ab,kw
#8	(Prednisone or Cortan or Cortancyl or Cutason or Dacortin or Decortisyl or Dehydrocortisone or delta-Cortisone or Deltasone or Encorton or Encortone or Enkortolon or Kortancyl or Liquid Pred or Meticorten or Orasone or Panafcort or Panasol or Predni Tablinen or Prednidib or Predniment or Prednison accis or Prednison Galen or Prednison Hexal or Pronisone or Rectodelt or Sone or Sterapred or Ultracorten or Winpred):ti,ab,kw
#9	(hydrocortisone or Cortifair or Cortisol or Cortril or Epicortisol):ti,ab,kw
#10	(adrenocorticotrophin):ti,ab,kw
#11	(fosphenytoin or Cerebyx or HMPDP or Prodilantin or ACC-9653 or 3- hydroxymethyl phenytoin disodium phosphate or 3 hydroxymethyl phenytoin phosphate ester):ti,ab,kw
#12	(isoflurane):ti,ab,kw
#13	(thiopentone or bomathal or penthiobarbital or pentothal or pentothal sodico or sodipental or thiomebumal or thionembutal or thiopentobarbital or thiopentone or tiobarbital braun or trapanal):ti,ab,kw
#14	(diazepam or 7-chloro-1 3-dihydro-1-methyl-5-phenyl-2h-1 4-benzodiazepin-2-one or apaurin or diazemuls or faustan or relanium or seduxen or sibazon or stesolid or valium):ti,ab,kw
#15	(eslicarbazepine acetate or S-licarbazepine or zebinix):ti,ab,kw
#16	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15

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2 **1.3.3 Pregnancy**

3 Which anti-epileptic drugs are clinically effective, cost-effective and safest for use in pregnancy?

4

Population	Intervention / exposure	Comparison	Study filters used	Date parameters
Epilepsy	Drugs	Each other or placebo	Systematic reviews, RCTs, observational	Start dates: Medline 1950, Embase 1980,

Population	Intervention / exposure	Comparison	Study filters used	Date parameters
			studies (Medline and Embase only)	Cinahl 1982 Searched up to: 03/06/10

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Medline & Embase search terms

1	(pregabalin or Lyrica or 3 isobutyl GABA).mp.
2	(rufinamide or CGP 33101 or 1 2 6 difluorobenzyl 1H 1 2 3 triazole 4 carboxamide).mp.
3	(zonisamide or Zonegran or AD 810 o 1 2 benzisoxazole 3 methanesulfonamide or 3 sulfamoylmethyl 1 2 benzisoxazole).mp.
4	(lacosamide or N-benzyl-2-acetamido-3-methoxypropionamide or N-benzyl-AcMeOPrNH2).mp.
5	(stiripentol or D-306).mp.
6	(nitrazepam or Alodorm or Dormalon or Dormo-Puren or Eatan or Imadorm or imeson or Mogadon or Nitrazadon or Nitrazep or Nitrodiazepam or Novanox or Radedorm or Remnos or Serenade or Somnite).mp.
7	(prednisolone or Di-Adreson-F or Predate or Predonine).mp.
8	(hydrocortisone or Cortifair or Cortisol or Cortril or Epicortisol).mp.
9	(Prednisone or Cortan or Cortancyl or Cutason or Dacortin or Decortisyl or Dehydrocortisone or delta-Cortisone or Deltasone or Encorton or Encortone or Enkortolon or Kortancyl or Liquid Pred or Meticorten or Orasone or Panafcort or Panasol or Predni Tablinen or Prednidib or Predniment or Prednison acsis or Prednison Galen or Prednison Hexal or Pronisone or Rectodelt or Sone or Sterapred or Ultracorten or Winpred).mp.
10	adrenocorticotrophin.mp.
11	(fosphenytoin or Cerebyx or HMPDP or Prodilantin or ACC-9653 or 3-hydroxymethyl phenytoin disodium phosphate or 3 hydroxymethyl phenytoin phosphate ester).mp.

12	isoflurane.mp.
13	(thiopentone or bomathal or penthiobarbital or pentothal or pentothal sodico or sodipental or thionembumal or thionembutal or thiopentobarbital or thiopentone or tiobarbital braun or trapanal).mp.
14	(diazepam or 7-chloro-1 3-dihydro-1-methyl-5-phenyl-2h-1 4-benzodiazepin-2-one or apaurin or diazemuls or faustan or relanium or seduxen or sibazon or stesolid or valium).mp.
15	(eslicarbazepine acetate or S-licarbazepine or zebinix).mp.
16	or/1-16

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2

Cinahl search terms

S1	pregabalin or Lyrica
S2	rufinamide or CGP 33101 or 1 2 6 difluorobenzyl 1H 1 2 3 triazole 4 carboxamide
S3	zonisamide or Zonegran or AD 810 o 1 2 benzisoxazole 3 methanesulfonamide or 3 sulfamoylmethyl 1 2 benzisoxazole
S4	lacosamide or N-benzyl-2-acetamido-3-methoxypropionamide or N-benzyl-AcMeOPrNH2
S5	stiripentol or D-306
S6	nitrazepam or Alodorm or Dormalon or Dormo-Puren or Eatan or Imadorm or imeson or Mogadon or Nitrazadon or Nitrazep or Nitrodiazepam or Novanox or Radedorm or Remnos or Serenade or Somnite
S7	prednisolone or Di-Adreson-F or Predate or Predonine
S8	Prednisone or Cortan or Cortancyl or Cutason or Dacortin or Decortisyl or Dehydrocortisone or delta-Cortisone or Deltasone or Encorton or Encortone or Enkortolon or Kortancyl or Liquid Pred or Meticorten or Orasone or Panafcort or Panasol or Predni Tablinen or Prednidib or Predniment or Prednison acsis or Prednison Galen or Prednison Hexal or Pronisone or Rectodelt or Sone or Sterapred or Ultracorten or Winpred
S9	hydrocortisone or Cortifair or Cortisol or Cortril or Epicortisol
S10	adrenocorticotrophin

S11	fosphenytoin or Cerebyx or HMPDP or Prodilantin or ACC-9653 or 3- hydroxymethyl phenytoin disodium phosphate or 3 hydroxymethyl phenytoin phosphate ester
S12	thiopentone or bomathal or penthiobarbital or pentothal or pentothal sodico or sodipental or thiomebutal or thionembutal or thiopentobarbital or thiopentone or tiobarbital braun or trapanal
S13	diazepam or 7-chloro-1 3-dihydro-1-methyl-5-phenyl-2h-1 4-benzodiazepin-2-one or apaurin or diazemuls or faustan or relanium or seduxen or sibazon or stesolid or valium
S14	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13

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Cochrane search terms – Wiley interface

#1	pregabalin or Lyrica
#2	(rufinamide or CGP 33101 or 1 2 6 difluorobenzyl 1H 1 2 3 triazole 4 carboxamide):ti,ab,kw
#3	(zonisamide or Zonegran or AD 810 o 1 2 benzisoxazole 3 methanesulfonamide or 3 sulfamoylmethyl 1 2 benzisoxazole):ti,ab,kw
#4	(lacosamide or N-benzyl-2-acetamido-3-methoxypropionamide or N-benzyl-AcMeOPrNH2):ti,ab,kw
#5	(stiripentol or D-306):ti,ab,kw
#6	(nitrazepam or Alodorm or Dormalon or Dormo-Puren or Eatan or Imadorm or imeson or Mogadon or Nitrazadon or Nitrazep or Nitrodiazepam or Novanox or Radedorm or Remnos or Serenade or Somnite):ti,ab,kw
#7	(prednisolone or Di-Adreson-F or Predate or Predonine):ti,ab,kw
#8	(Prednisone or Cortan or Cortancyl or Cutason or Dacortin or Decortisyl or Dehydrocortisone or delta-Cortisone or Deltasone or Encorton or Encortone or Enkortolon or Kortancyl or Liquid Pred or Meticorten or Orasone or Panafcort or Panasol or Predni Tablinen or Prednidib or Predniment or Prednison accis or Prednison Galen or Prednison Hexal or Pronisone or Rectodelt or Sone or Steraped or Ultracorten or Winpred):ti,ab,kw
#9	(hydrocortisone or Cortifair or Cortisol or Cortril or Epicortisol):ti,ab,kw
#10	(adrenocorticotrophin):ti,ab,kw
#11	(fosphenytoin or Cerebyx or HMPDP or Prodilantin or ACC-9653 or 3- hydroxymethyl

	phenytoin disodium phosphate or 3 hydroxymethyl phenytoin phosphate ester):ti,ab,kw
#12	(isoflurane):ti,ab,kw
#13	(thiopentone or bomathal or penthiobarbital or pentothal or pentothal sodico or sodipental or thiomebumal or thionembulal or thiopentobarbital or thiopentone or tiobarbital braun or trapanal):ti,ab,kw
#14	(diazepam or 7-chloro-1 3-dihydro-1-methyl-5-phenyl-2h-1 4-benzodiazepin-2-one or apaurin or diazemuls or faustan or relanium or seduxen or sibazon or stesolid or valium):ti,ab,kw
#15	(eslicarbazepine acetate or S-licarbazepine or zebinix):ti,ab,kw
#16	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15

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2 **1.3.4 Economics Search**

3 Economic searches were conducted in Medline, Embase and CRD for EED and HTA

4

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Stable COPD			Economic (Medline and Embase only)	Medline and Embase 2007-24/7/09 CRD EED and HTA 2003-24/7/09

5

6

7 **Medline economic filter search terms**

- 8 1. costs.tw.
 9 2. cost effective.tw.
 10 3. economic.tw.
 11 4. 1 or 2 or 3
 12 5. (metabolic adj cost).tw.

- 1 6. ((energy or oxygen) adj cost).tw.
- 2 7. 5 or 6
- 3 8. 4 not 7

4
5 **Embase economic filter search terms**

- 6 1. costs.tw.
- 7 2. cost effective.tw.
- 8 3. economic.tw.
- 9 4. 1 or 2 or 3
- 10 5. (metabolic adj cost).tw.
- 11 6. ((energy or oxygen) adj cost).tw.
- 12 7. 5 or 6
- 13 8. 4 not 7

14
15 **COPD CRD search terms**

16 chronic obstructive pulmonary disease or COPD

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18
19
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