BIBLIOGRAPHIC REFERENCE TABLE FOR CARBAMAZEPINE IN CHILDHOOD EPILEPSY

Bibliographic reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect size	Source of funding	Additional comments
Tudur Smith C et al. Carbamazepine versus phenobarbitone monotherapy for epilepsy (Review). The Cochrane Collaboration 2003	Systematic review of randomised or quasi-randomised, blinded or non-blinded controlled trials	684	Children and adults	To assess the effects of carbamazepine compared with phenobarbitone for people with partial onset seizures (simple/complex partial or secondarily generalized seizures) or generalized onset tonic-clonic seizures (with or without other generalized seizure types)	Carbamazepine with phenobarbitone	12 months	Time to withdrawal of allocated treatment (due to lack of efficacy or intolerable adverse effects); time to 12 month remission; time to first seizure	Data were analysed using a stratified logrank analysis with results expressed as hazard ratios (HR) and 95% confidence intervals (CIs) where a HR >1 indicates an event is more likely on phenobarbitone. The main overall results were (i) time to withdrawal 1.63 (1.23 to 2.15). (ii) time to 12 month remission 0.87 (0.65 to 1.17), (iii) time to first seizure 0.85 (0.68-1.05)	No sources of support supplied	Review suggests that time to withdrawal is significantly improved with carbamazepine compared to phenobarbitone. No overall difference between drugs is identified for the other outcomes. Statistical heterogeneity was not encountered.
Marson AG et al. Carbamazepine versus valproate monotherapy for epilepsy (Review). The Cochrane Collaboration 2000	Systematic review of randomized controlled monotherapy studies; studies may be double, single or unblinded	1256	Children and adults	To compare the efficacy and tolerability of carbamazepine and valproate when used as monotherapy in people with partial onset seizures (simple partial, complex partial or secondarily generalizing	Carbamazepine with valproate	12 months	Time to withdrawal of allocated treatment (due to lack of efficacy or intolerable adverse effects); time to 12 month remission; time to first seizure	Data were analysed using a stratified logrank analysis with results expressed as hazard ratios (HR) and 95% confidence intervals (CIs) where a HR >1 indicates an event is more likely on	External sources of support - Wellcome Trust UK; Medical Research Council UK	Results suggest no overall difference for the outcome measures described. The test for an interaction between seizure type was non-significant for time to treatment

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				tonic-clonic seizures) or generalized onset tonic-clonic seizures				valproate. The main overall results (HR) were: time to treatment withdrawal 0.97 (95% CI 0.79-1.18); 12 month remission 0.87 (95% CI 0.74-1.02); first seizure 1.09 (95% CI 0.96-1.25)		withdrawal and 12-month remission, but significant for time to first seizure.
De Silva M et al. Randomised comparative monotherapy trial of phenobarbitone, phenytoin, carbamazepine or sodium valproate for newly diagnosed childhood epilepsy. Lancet, 1996; 347: 709-713	Randomised, prospective long-term clinical trial	167	Children aged 3-16 years	To compare the efficacy and toxicity of phenobarbitone, phenytoin, carbamazpeine and sodium valproate as monotherapy in children with newly diagnosed epilepsy	To compare the efficacy and toxicity of phenobarbitone, phenytoin, carbamazpeine and sodium valproate as monotherapy	44 months (range 3-88)	Time to first seizure; time to achieve a 1-year remission from all seizures	Significant difference between the groups in the proportion of children withdrawn from the randomized drugs because of unacceptable side-effects (X^2 = 35.1, P=0.001). Patients in phenobarbitone group were more likely to have the drug withdrawn than those in the other groups (X^2 = 33.9, p<0.001; odds ratio 24.7 95% CI 4.9-133). No significant difference in the proportion of patients withdrawn	Ciba-Geigy, Parke-Davis and Sanofi	Overall outcome with all 4 drugs was good. Phenobarbitone showed an unacceptable incidence of side-effects that necessitated withdrawal of this treatment. all

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								between the other 3 groups. Overall analysis for the 167 children showed that by 3 years of follow-up, 20% (95% CI 13-26) had remained seizure free and 73% had achieved a 1 year remission.		
Tudur Smith C et al. Carbamazepine versus phenytoin monotherapy for epilepsy (Review) The Cochrane Collaboration 2002	Systematic review of randomized parallel group monotherapy trials. Studies may be double-blind, single blind or unblended with adequate or quasi methods of randomisation	551	Adults and children	To review the best evidence comparing carbamazepine and phenytoin when used as monotherapy in patients with partial onset seizures (simple partial, complex partial or secondarily generalised tonic-clonic seizures) or generalized onset tonic-clonic seizures (with or without other generalized seizure types)	Carbamazepine with phenytoin as monotherapy	12 months	Time to withdrawal of allocated treatment; time to 12 month remission; time to 6 month remission; time to first seizure post randomisation	Data were analysed using a stratified logrank analysis with results expressed as hazard ratios (HR) and 95% confidence intervals (CIs) where a HR >1 indicates an event is more likely on phenytoin. Time to withdrawal of allocated treatment 0.97 (95% CI 0.74 to 1.28); time to 12 month remission 1.00 (95% CI 0.78 to 1.29); time to 6 month remission 1.10 (95% CI 0.87 to 1.39) and time to first seizure	External sources of support – Medical Research Council UK	Results suggest no overall difference between carbamazepine and phenytoin for these outcomes

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								0.91 (95% CI 0.74 to 1.12)		
Verity CM et al. A multicentre comparative trial of sodium valproate and carbamazepine in paediatric epilepsy. Dev Med Child Neurol 195; 37(2): 97-108	Randomised multicentre comparative trial	260	Children aged 5-16 years	To assess the long-term efficacy and side-effect profiles of sodium valproate and carbamazepine in children with primary generalized epilepsy (with or without secondary generalization)	Carbamazepine versus sodium valproate monotherapy	3 years	Efficacy (remission analyses at 6, 12 and 24 months) and tolerability of treatments	Remission analyses produced no statistically significant treatment difference between treatments at 6 months (RR 0.98; p=0.91; 95% CI 73 to 1.32); a marginal but non-significant advantage for sodium valproate in 12 month remission (RR 1.05; p=0.75; 95% CI 0.76 to 1.46) and a larger but still statistically insignificant advantage for sodium valproate in 24 month remission (RR 1.44; p=0.10; 95% CI 0.93-2.21) Both drugs achieved a high degree of seizure control with 75% of patients having	Sanofi Winthrop	Little difference in overall efficacy between the drugs. Analysis of treatment failures showed there was little difference in failure rates between the drugs.

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								at least 12 months and 45-55% at least 2 years of freedom from seizures.		
Gamble CL et al. Lamotrigine versus carbamazepine monotherapy for epilepsy (Review). The Cochrane Collaboration2006	Systematic review of randomized controlled trials (double, single or unblended with adequate methods of randomization)	1384	Adults and children	To review the best evidence comparing carbamazepine and lamotrigine when used as monotherapy in people with partial onset seizures or generalized onset tonic-clonic seizures with or without other generalized seizure types	Carbamazepine and lamotrigine monotherapy	6 months	Time to treatment withdrawal; time to first seizure post randomization; seizure freedom at 6 months	Time to event data were analysed using a stratified logrank analysis with results expressed as hazard ratios and 95% CI. A HR or a RR greater than 1 indicated an event was more likely on lamotrigine than carbamazepine. Time to treatment withdrawal 0.55 (95% CI 0.35 to 0.84); time to first seizure post randomization 1.14 (95% CI 0.92 to 1.43)	No sources of support supplied	Lamotrigine was significantly less likely to be withdrawn than carbamazepine but results for time to first seizure suggest that carbamazepine may be superior in terms of seizure control
Brodie MJ et al. Double-blind comparison of lamotrigine and carbamazepine in newly diagnosed epilepsy. Lancet 1995; 345: 476-479	Double-blind randomized parallel group study	260	Adults and children over 13 years	To investigate lamotrigine in comparison with carbamazepine in patients with newly diagnosed epilepsy presenting with partial or generalized tonic-clonic	Lamotrigine versus carbamazepine monotherapy	48 weeks	Time to first seizure; time to withdrawal	No significant difference between the drugs in time to first seizure after 6 weeks treatment (HR 0.8 CI 0.6-.21). Only adverse effects for which there was a significant	Wellcome Foundation	Lamotrigine and carbamazepine showed similar efficacy against partial onset seizures and primary generalized tonic-clonic seizures. Lamotrigine was better

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				seizures or both				difference in frequency between the 2 groups was sleepiness which was significantly more likely with carbamazepine ($p<0.05$). A greater proportion of the lamotrigine group completed the study (65% vs 51% $p=0.018$)		tolerated.
Chadwick D. Safety and efficacy of vigabatrin and carbamazepine in newly diagnosed epilepsy: a multicentre randomized double blind study. Lancet 1999; 354: 13-19	Multicentre randomized double blind study	459	12-65 years	To investigate whether vigabatrin was comparable to standard first line monotherapy in efficacy and incidence of adverse events in patients with newly diagnosed partial epileptic seizures	Vigabatrin versus carbamazepine monotherapy	52 weeks(then some continued in open trial)	Primary outcome – time to withdrawal because of lack of efficacy or adverse effects; secondary outcome were efficacy (time to 6 month remission; time to first seizure after initial dose stabilization)	Time to withdrawal for lack of efficacy did not differ between groups ($p=0.318$). Vigabatrin better tolerated than carbamazepine with fewer withdrawals due to adverse effects. All efficacy outcomes favoured carbamazepine. No significant difference found for time to achieve 6 months of remission from seizures ($p=0.058$) but time to first	Hoechst Marion Roussell	Vigabatrin is less effective but seems better tolerated than carbamazepine

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								seizure after the first 6 months of randomization showed carbamazepine to be significantly more effective than vigabatrin (p=0.0001)		
Wheless JW et al. Topiramate, carbamazepine and valproate montherapy: double blind comparison in children with newly diagnosed epilepsy. J Child Neurol, 2004; 19(2): 135-141	Randomised, double-blind multicentre trial	613 (of whom 119 were children or adolescents)	Adults and children (6-16 years)	To compare the efficacy of topiramate monotherapy with carbamazepine and valproate as first line therapy in patients with newly diagnosed epilepsy	Topiramate with carbamazepine and valproate	Variable since treatment was continued until the patients exited or until 6 months after the last patient was enrolled.	Efficacy and tolerability/safety	For the paediatric subsection – efficacy analyses showed no statistically significant differences between topiramate and carbamazepine or valproate. Fewer patients in the carbamazepine and topiramate groups discontinued treatment due to adverse effects compared to valproate	Johnson and Johnson Pharmaceutical Research	For the paediatric subsection – efficacy analyses showed no statistically significant differences between topiramate and carbamazepine or valproate.