

National Essential Drug List Medication Review Process

Primary Healthcare

Component: Central nervous system conditions

Date: July 2013

Medication: Lamotrigine

Indication: General tonic clonic seizures and used concomitantly with ARVs.

Background:

Lamotrigine was launched for adjunctive treatment of epilepsy in 1991 and licensed for use as monotherapy in 1995. Its indications include partial seizures and primary and secondarily generalised tonic–clonic seizures.

Lamotrigine is not licensed as monotherapy for children younger than 12 years; as combination therapy, it is licensed for both adults and children older than 2 years.

Evidence:

Evidence from five randomised controlled trials including children was reviewed in the Assessment Report¹.

One of them was a comparison of lamotrigine monotherapy with carbamazepine in newly diagnosed partial seizures (n = 417 randomised to lamotrigine or carbamazepine in a 2:1 ratio)². As monotherapy in partial seizures, the comparison with carbamazepine found no statistically significant differences in terms of seizure outcomes between the two drugs. This was a mixed age study of patients aged 2 years and older, but results for the children 12 years and younger (n = 233) were reported separately. In the paediatric subpopulation, there was a much smaller difference in withdrawals due to adverse effects (5% for lamotrigine and 7% for carbamazepine), which was not statistically significant. This study provides evidence for the effectiveness of lamotrigine monotherapy in partial seizures, but it cannot be concluded that lamotrigine and carbamazepine are equivalent.

The clinical trial³ of adjunctive lamotrigine in partial seizures included children between the ages of 2 and 16 years. This study provided evidence that lamotrigine was superior to placebo in suppressing seizures in patients who had not become seizure-free on their existing therapy. There was a greater reduction in median seizure frequency in the lamotrigine group than in the placebo group: a 36.1% reduction compared with a 6.7% reduction in the placebo group over

¹ NICE Guidance TA079: Newer drugs for epilepsy in children, April 2004

² Nieto-Barrera M, Brozmanova M, Capovilla G, Christie W, Pedersen B, Kane K, O'Neill F; Lamictal vs. Carbamazepine Study Group. A comparison of monotherapy with lamotrigine or carbamazepine in patients with newly diagnosed partial epilepsy. *Epilepsy Res.* 2001 Aug;46(2):145-55.

³ Duchowny M, Pellock JM, Graf WD, Billard C, Gilman J, Casale E, Womble G, Risner M, Manasco P. A placebo-controlled trial of lamotrigine add-on therapy for partial seizures in children. *Lamictal Pediatric Partial Seizure Study Group. Neurology.* 1999 Nov 10;53(8):1724-31.

the 18-week follow-up period (6 weeks' dose titration plus a 12-week maintenance period). This was statistically significant, $p = 0.008$.

There is not much evidence that has compared lamotrigine and older AED monotherapy in the management of generalised tonic-clonic seizures in children.

Additional references

Gamble CL, Williamson PR, Marson AG. Lamotrigine versus carbamazepine monotherapy for epilepsy. *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD001031.

The conclusion of the SANAD 2007⁴ study arm, comparing valproate, lamotrigine and topiramate for generalised seizures was that valproate should remain the drug of choice for generalised and unclassifiable epilepsy³. In the latter study, valproate was better tolerated than topiramate and more efficacious than lamotrigine. There was however insufficient power to make definitive statements about the relative efficacy and effectiveness of the drugs for individual seizure types and subsyndromes.

⁴ Marson AG, Al-Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, Cramp C, Cockerell OC, Cooper PN, Doughty J, Eaton B, Gamble C, Goulding PJ, Howell SJ, Hughes A, Jackson M, Jacoby A, Kellett M, Lawson GR, Leach JP, Nicolaidis P, Roberts R, Shackley P, Shen J, Smith DF, Smith PE, Smith CT, Vanoli A, Williamson PR; SANAD Study group. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. *Lancet*. 2007 Mar 24;369(9566):1016-26.