

A new era of seizure control starts here . . .

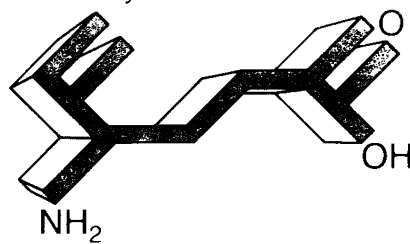
...with a rationally designed anti-epileptic

A new anti-epileptic, SABRIL (vigabatrin) has been launched for patients with uncontrolled seizures.

SABRIL, designed to increase levels of the inhibitory neurotransmitter GABA, is a specific GABA-T inhibitor effective in epilepsy.

Numerous studies confirm that SABRIL is clinically effective in 50% of patients with uncontrolled epilepsy (1,2,3). SABRIL is particularly effective in reducing the incidence and/or severity of partial seizures (2,3). This efficacy is maintained in the long-term (4).

Tolerability has been confirmed in over 1200 epilepsy patients treated with SABRIL (1). SABRIL is well tolerated (1) and blood level monitoring is not required.



SABRIL[®]

VIGABATRIN

Specific GABA-transaminase inhibition
for uncontrolled epilepsy

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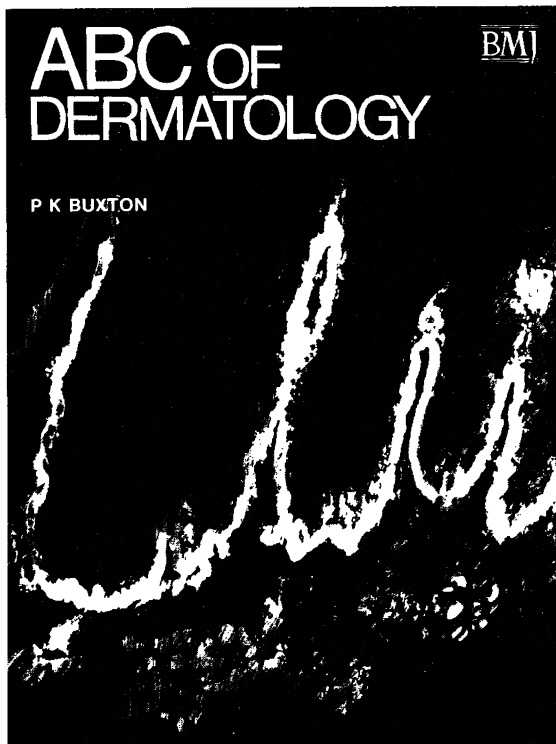
Merrell Dow Pharmaceuticals Limited, 1 Furzegrund Way, Stockley Park, Uxbridge, Middx. UB11 1BE.

TRADEMARKS: Sabril, Merrell, Dow. Abridged Prescribing Information and references appear on the following page.

Sabril Abridged Prescribing Information ▼

Presentation White, oval biconvex tablets with a breakline on one side and SABRIL on the other. Each tablet contains 500 mg vigabatrin. **Uses Mode of Action** A selective, irreversible inhibitor of GABA-transaminase. Treatment leads to an increase in brain levels of GABA (gamma aminobutyric acid). **Indications** Indicated for the treatment of epilepsy which is not satisfactorily controlled by other antiepileptic drugs. **Dosage and Administration** For oral administration once or twice daily and may be taken before or after meals. **Adults:** The recommended daily starting dose is 2 g (4 tablets) which should be added to the patient's current therapeutic regimen. The dose may be increased or decreased in 0.5 g or 1.0 g increments depending upon clinical response and tolerability. Increasing the dose above 4g/day does not usually result in improved efficacy. There is no direct correlation between plasma concentration and efficacy. The duration of the effects of the drug are dependent on the rate of enzyme resynthesis rather than the concentration of drug in the plasma. **Children:** The recommended daily starting dose is 1g (2 tablets) in children aged 3-9 years and 2g (4 tablets) in older children. **Elderly:** Dosage reduction may be necessary in patients with impaired renal function, particularly patients with creatinine clearance less than 60 ml/min. See 'Precautions.' **Contra-indications, Precautions, Warnings etc.** Use of Sabril during pregnancy and lactation: Use of Sabril during pregnancy is contra-indicated. There is no evidence of the safety of Sabril treatment whilst breast-feeding and so it is not recommended. **Precautions:** As with other antiepileptic drugs abrupt withdrawal may lead to rebound seizures. If treatment is to be discontinued it is recommended that this is done by gradually reducing the dose over 2-4 weeks. Caution should be exercised when administering the product to elderly patients and more particularly patients with creatinine clearance of less than 60 ml/min. Reduced doses should be used and patients monitored closely for adverse events such as sedation and confusion. **Warnings:** Animal safety studies indicate that vigabatrin causes intramyelinic oedema in the brain white matter tracts. Currently there is no evidence to suggest that this effect occurs in man. However, it is recommended that patients treated with Sabril are closely observed for adverse effects on neurological function. Details of animal findings are given under "Further Information" in the full product data sheet. **Effects on driving ability:** Drowsiness has been observed and patients should be warned of this possibility before treatment. Special care should be taken by patients driving, operating machinery or performing any hazardous task. **Side-effects:** Adverse events are mainly CNS related. The following events have been reported but in most cases the relationship to vigabatrin has not been established: drowsiness and fatigue, dizziness, nervousness, irritability, depression, headache and less commonly confusion, psychosis, memory disturbance and vision complaints such as diplopia. Other adverse events reported include weight gain and minor gastrointestinal side-effects. In children excitation and agitation have been seen. The sedative effect of vigabatrin decreases with continuing treatment. As with other antiepileptic drugs, some patients may experience an increase in seizure frequency with vigabatrin. Patients with myoclonic seizures may be particularly liable to this effect. There is no evidence of neurotoxicity in humans. Tests done to confirm lack of significant adverse effect on neurological function include evoked potentials, CAT scans, magnetic resonance imaging, CSF analyses and in a small number of cases, neuropathological examinations of brain specimens. Laboratory data indicate that Sabril treatment does not lead to renal or hepatic toxicity. Decreases in SGOT and SGPT have been observed and may be a result of inhibition of these transaminases by Sabril. Chronic treatment with Sabril may be associated with a slight decrease in haemoglobin which rarely attains clinical significance. **Drug Interactions:** Sabril is not metabolised, or protein bound and does not induce hepatic cytochrome P450 or drug metabolising enzymes so interactions with other drugs are unlikely. In clinical studies a gradual reduction of about 20% in plasma phenytoin concentration has been observed. The mechanism is not understood but this is unlikely to be of therapeutic significance. No clinically significant interactions have been seen with carbamazepine, phenobarbitone or sodium valproate in clinical trials. **Overdose:** There is no specific antidote and the usual supportive measures should be employed. Overdoses of 14 and 30g of Sabril have been reported without any sequelae. **Pharmaceutical Precautions** None. **Legal Category** POM. **Package Quantities** Blister strips of 10 in cartons of 100. **Product Licence Number:** PL 4425/0098. **NHS Price:** pack of 100 tabs. £46.00. **Date of Preparation:** October 1989. You must refer to the full prescribing information before administering Sabril. Further information including full product data sheet is available from the Licence Holder: Merrell Dow Pharmaceuticals Ltd., 1, Furzeground Way, Stockley Park, Uxbridge, Middx UB11 1BE. 1. Browne TR et al. Neurology 1987; 37: 184-189. 2. Mumford JP Br J Clin Pract 1988, 42 (Suppl 61): 7-9. 3. Pedersen SA et al Acta Neurol Scan 1985; 72: 295-298. 4. Remy C, Beaumont DBR J Clin Pharmac (1989) 27, 125S-129S.

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Vol 3, 1990, No 1

No 1	THIS ISSUE	February
No 1	Coma, intracranial pressure, intensive care, head injury and neoplasia. M Salzman Cerebrovascular disease. G Ferguson Neuropsychology, dementia and aging. A Bertozzi	
No 2	Infectious and demyelinating disease. Pain and disorders of consciousness	April
No 3	Extrapontine developmental and inherited CNS disease. Pediatric neurology. Metabolic disorders and neurotoxicology	June
No 4	Autonomic disorders. Neuropharmacology. Disorders of the spinal cord	August
No 5	Neuromuscular disease. Neurological rehabilitation. Clinical neurophysiology, neuro-otology and neuro-ophthalmology	October
No 6	Neuroimaging. Dynamic neuropathology. Clinical neurochemistry	December

Volume 2 Number 1 February 1989

Coma, intracranial pressure, intensive care, head injury and neoplasia

edited by M. Salzman

M. Salzman Editorial review
J.J. Cole Coma
E.J. Rutledge and J.M. Lundberg Intensive care of head injury
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Cerebrovascular disease

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R.W. Ross Russell Editorial review
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R.W. Wolf The pathophysiology of cerebral ischemia and stroke
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G. Loring The neurosurgical treatment of cerebral vascular conditions

The non-surgical treatment of cerebral aneurysms

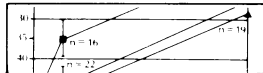
J.C. Grotta

Department of Neurology, University of Texas Medical School, Houston, Texas, USA

Current Opinion in Neurology and Neurosurgery 1989; 2:66-72

Introduction

Progress in the medical prevention and therapy of cerebral ischemia continues at a rapid pace. In prevention, the role of aspirin has been clarified, but questions remain about proper dose, and its lipoline is emerging as a promising new drug. In treatment, pilot studies of cal-



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or the determination of the influence of blood glucose levels on the risk of neurologic complications in 54 infants undergoing intracardiac surgery. Demonstration of a trend suggesting a deleterious effect of dextrose infusions during pediatric cardiac surgery.

17. VOS, RUTHEN, G.M., HEIJER, A., BUNSTED, M.D., SCHLESKER, A. ● Transcranial Doppler ultrasonography during cardiopulmonary bypass in patients with severe carotid stenosis or occlusion. *Stroke* 1988; 19:674-681.

Monitoring of middle cerebral artery blood flow velocity by transcranial Doppler during CPB in patients with 100% and without 42% severe carotid stenosis or occlusion. Demonstrates no reduced perfusion and argues once more against the policy of systematic carotid endarterectomy prior to cardiac surgery in this situation.

18. MURKIN, J.M., FARBER, J.K., TREFF, W.A., MCKENZIE, E.S., GURDIN, G. ● Cerebral autoregulation and flow metabolism coupling during cardiopulmonary bypass: the influence of PaCO₂. *Anesth Analg* 1987; 66:825-832.

Study of cerebral blood flow and oxygen consumption in 36 patients undergoing CPB with emphasis on the effect of maintaining a temperature corrected or non corrected PaCO₂ of 40 mmHg on these parameters. First oxygen metabolism study in this situation. Demonstration of a 75% reduction in CMRO₂ and of better preserved flow metabolism

Current world literature

formulation for Canadian medicine. *Can Med Assoc J* 1988; 138:405-406 [25].

DARBY, J.M., YONAS, H., GUR, D., LATCHAW, R.E. ● Xenon-enhanced computed tomography in brain death. *Arch Neurol* 1987; 44:551-554.

DEMARIA, E.J., KENNEY, P.R., MERRIMAN, M.A., CASANOVA, L.A., GANN, D.S. ● Aggressive trauma care benefits the elderly. *J Trauma* 1987; 27:1200-1206.

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