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Sandomigran
or reduces its frequency significant

Prophylaxis of migraine: the problem.

The prophylactic treatment of vascular headaches has been hampered sometimes by the fact that the most effective agent (methysergide) for the prevention of migraine is associated with certain undesirable side effects. Because of this, the prophylactic therapy of migraine has been confined to a relatively small, select group of patients.

Overcoming the problem.

Extensive research and wide clinical experience have shown that Sandomigran is a highly effective agent against migraine. *Chemically unrelated to methysergide,* Sandomigran is free of the undesirable side effects which have sometimes interfered with or precluded the prophylactic treatment of vascular headaches.

The pharmacological properties of Sandomigran.

Migraine or vascular headache is not, according to many investigators, purely of vascular origin. Many researchers believe that the biogenic amines play an important role in the pathogenesis of migraine.
Chemically unrelated to methysergide, Sandomigran (pizotyline) is a benzocycloheptathiophene derivative possessing strong antagonistic action against certain biogenic amines such as serotonin and histamine and, to a lesser degree, tryptamine, acetylcholine and the catecholamines.
Sandomigran is indicated in the prophylactic — not the symptomatic — treatment of vascular headaches.

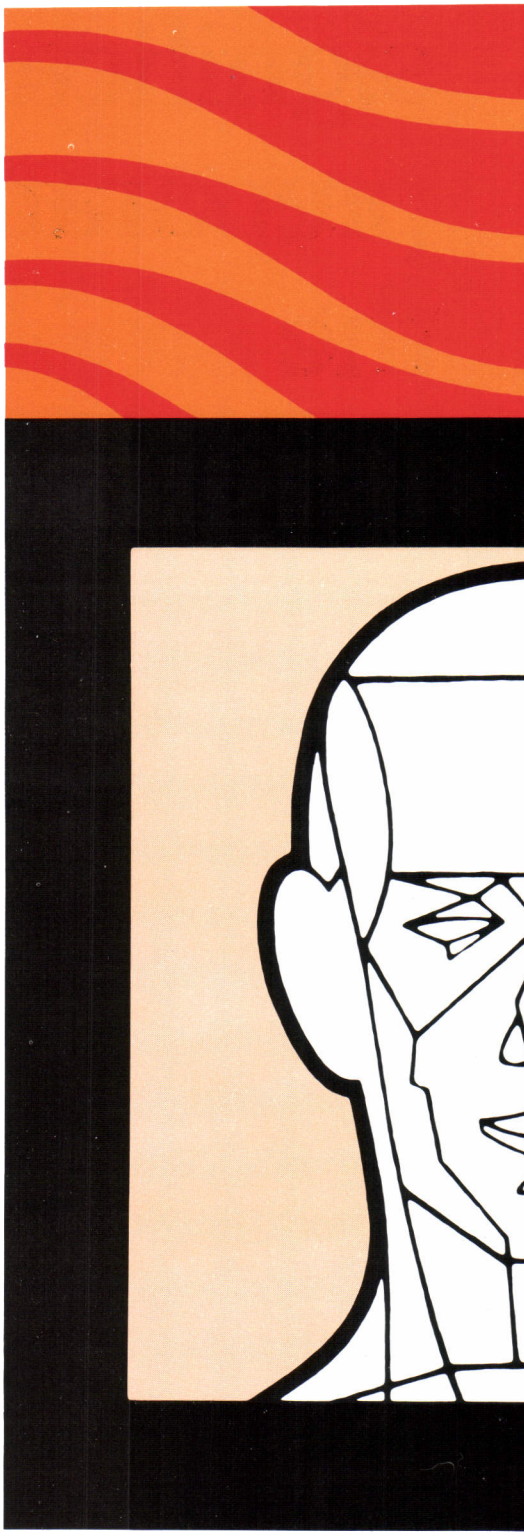
Patient selection.

Sandomigran should be considered primarily for the more serious cases of migraine; patients who suffer two or more severe headaches every month.
Sandomigran should also be considered for patients whose headaches do not respond to symptomatic treatment.

7 of every 10 migraine patients may benefit from Sandomigran.

An analysis of 10 controlled studies [1–10] (392 patients) shows the following gratifying results:

Excellent results (Complete disappearance of headaches) Good results (Reduction in frequency and severity of headaches by at least 50%)	65%



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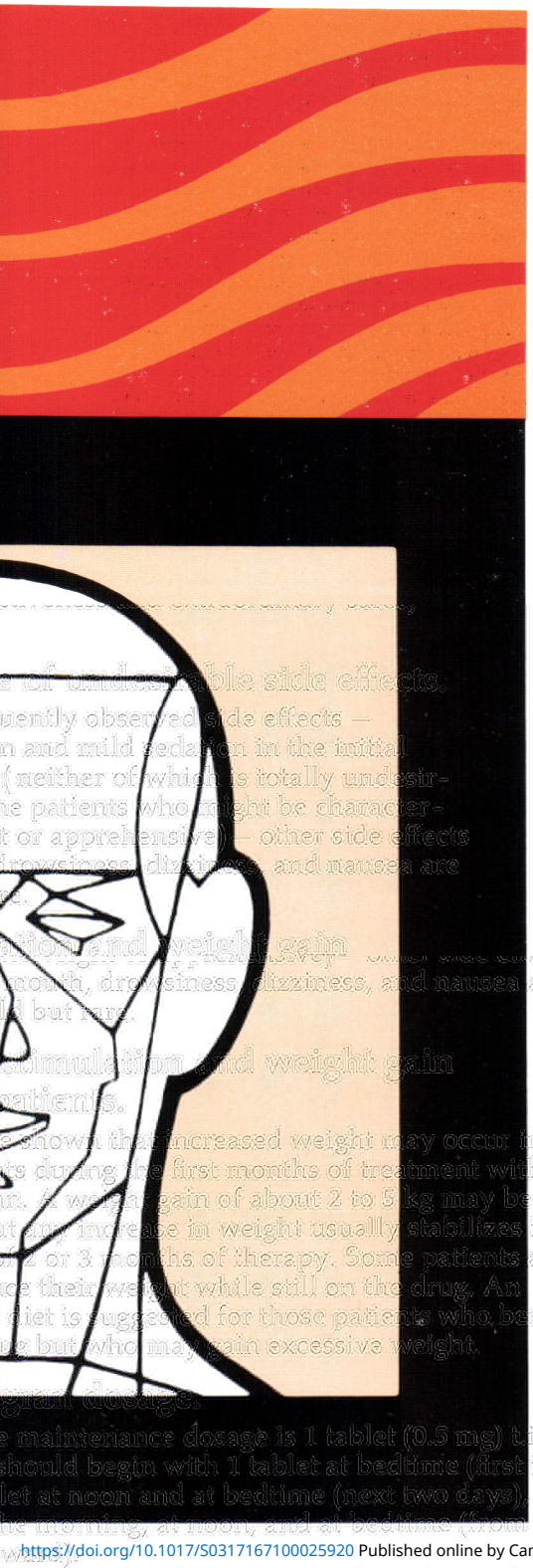
prevents migraine, and severity, without side effects.



Moderate results (Reduction in frequency and severity of headaches by an appreciable degree, but not reaching the aforementioned standards)	10%

Long-term effectiveness and safety of Sandomigran.

Sandomigran may be prescribed confidently for more migraine patients than ever before. A continuum of international data, based on up to 5 years of clinical experience in 60 countries, provides convincing evidence of the sustained effectiveness and extraordinary safety of Sandomigran.

Remarkably free of undesirable side effects.

Apart from two frequently observed side effects — moderate weight gain and mild sedation in the initial phase of treatment (neither of which is totally undesirable in some migraine patients who might be characteristically underweight or apprehensive) — other side effects such as dry mouth, drowsiness, dizziness, and nausea are not only mild but rare.

Appetite stimulation and weight gain in some patients.

Studies have shown that increased weight may occur in some patients during the first months of treatment with Sandomigran. A weight gain of about 2 to 5 kg may be observed but any increase in weight usually stabilizes in the course of 2 or 3 months of therapy. Some patients are able to reduce their weight while still on the drug. An appropriate diet is suggested for those patients who benefit from the drug but who may gain excessive weight.

Sandomigran dosage.

The average maintenance dosage is 1 tablet (0.5 mg) t.i.d. Treatment should begin with 1 tablet at bedtime (first two days), 1 tablet at noon and at bedtime (next two days), and 1 tablet in the morning, at noon, and at bedtime (from the fifth day onward).
Most investigators agree that a four week-trial period is required to determine the true efficacy of the drug in any given patient.

NEW

Sandomigran®

stops migraine before it attacks

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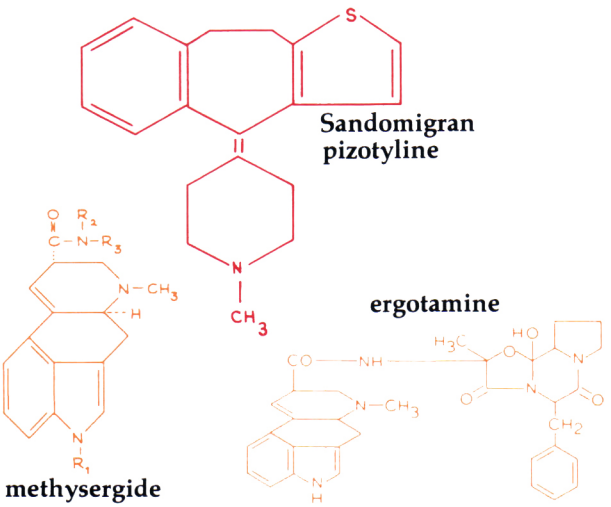
NEW Sandomigran®

PIZOTYLINE

Chemistry

The chemical structure of pizotyline (Sandomigran) is totally different to the chemical structure of either methysergide (Sansert) or ergotamine.



Sandomigran pizotyline

methysergide

ergotamine

Prescribing information

Dosage – The average maintenance dosage is 1 tablet (0.5 mg) t.i.d. A progressive dosage is recommended until the fifth day of therapy. Treatment should begin with 1 (0.5 mg) tablet at bedtime (first two days), 1 tablet at noon, and at bedtime (next two days), and 1 tablet in the morning, at noon, and at bedtime (from the fifth day onward). The dosage range is 2 to 12 tablets (1 to 6 mg) per day.
Since vascular headache is a paroxysmal but basically chronic disorder, treatment must extend over an adequate period of time in order to obtain maximal benefit. While some patients have responded rather quickly, most investigators agree that a four-week trial period should be instituted to determine the true efficacy of pizotyline in specific cases. The periodic nature of the disorder will have to be considered in determining when and for how long therapy should be maintained.
Since some investigators have observed a change in headache pattern after several months of therapy, a drug-free interval is advisable to reassess the necessity of continuing treatment. The dosage should be reduced gradually during the last two weeks of each treatment course to avoid a "headache rebound."
Composition – Each ivory-coloured, sugar coated tablet contains 0.5 mg of pizotyline as the hydrogen malate.

Side effects – Increased appetite, weight gain, and drowsiness are the most frequent side effects. An appropriate diet should be recommended by the physician for patients benefiting from the drug but gaining excessive weight. A gradual increase in the dosage of pizotyline is recommended to minimize or reduce the incidence of drowsiness.
The following adverse effects have been observed less frequently in relation to the aforementioned reactions: fatigue, nausea, dizziness, headache, confusion, edema, hypotension, depression, weakness, epigastric distress, dry mouth, nervousness, impotence and muscle pain.
Warnings and precautions – Since drowsiness may occur with pizotyline, sensitive patients should be cautioned against activities requiring rapid and precise responses (i.e. driving an automobile or operating dangerous machinery) until their response to the drug has been determined. Since the effects of antihistamines can potentiate those of other drugs affecting the central nervous system, patients should be cautioned against drinking alcoholic beverages or taking hypnotics, sedatives, psychotherapeutic agents or other drugs with CNS depressant effects during pizotyline therapy.
Since it is desirable to keep drug administration to a minimum during pregnancy, pizotyline should be given only when the benefits derived from treatment exceed the possible risks to mother and fetus.
Some patients developed tolerance to pizotyline with prolonged use of the drug. An increase in dosage may overcome this tolerance.
After prolonged use hepatotoxic effects might occur and patients should be advised to report for adequate laboratory evaluation.
Patients with diabetes, cardiovascular disease and known or suspected impaired renal or hepatic function should be given pizotyline with caution, and appropriate laboratory tests should be done at regular intervals.
Lens opacities occurred in two cases but did not appear to be drug-related. However, it is recommended that any impairment in vision be reported to the attending physician for further investigation.
Contraindications – Glaucoma, pyloroduodenal obstruction, stenosing pyloric ulcer and predisposition to urinary retention. Pizotyline is also contraindicated in patients taking monoamine oxidase inhibitors and for patients who have a known sensitivity to the drug. Until further studies are completed, the drug is not recommended for children under the age of twelve.

Supply – Bottles of 100 tablets.

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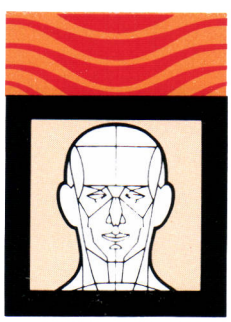
Full prescribing information is available upon request.



stops migraine before it attacks

SANDOZ

SANDOZ (CANADA) LIMITED, DORVAL, QUEBEC

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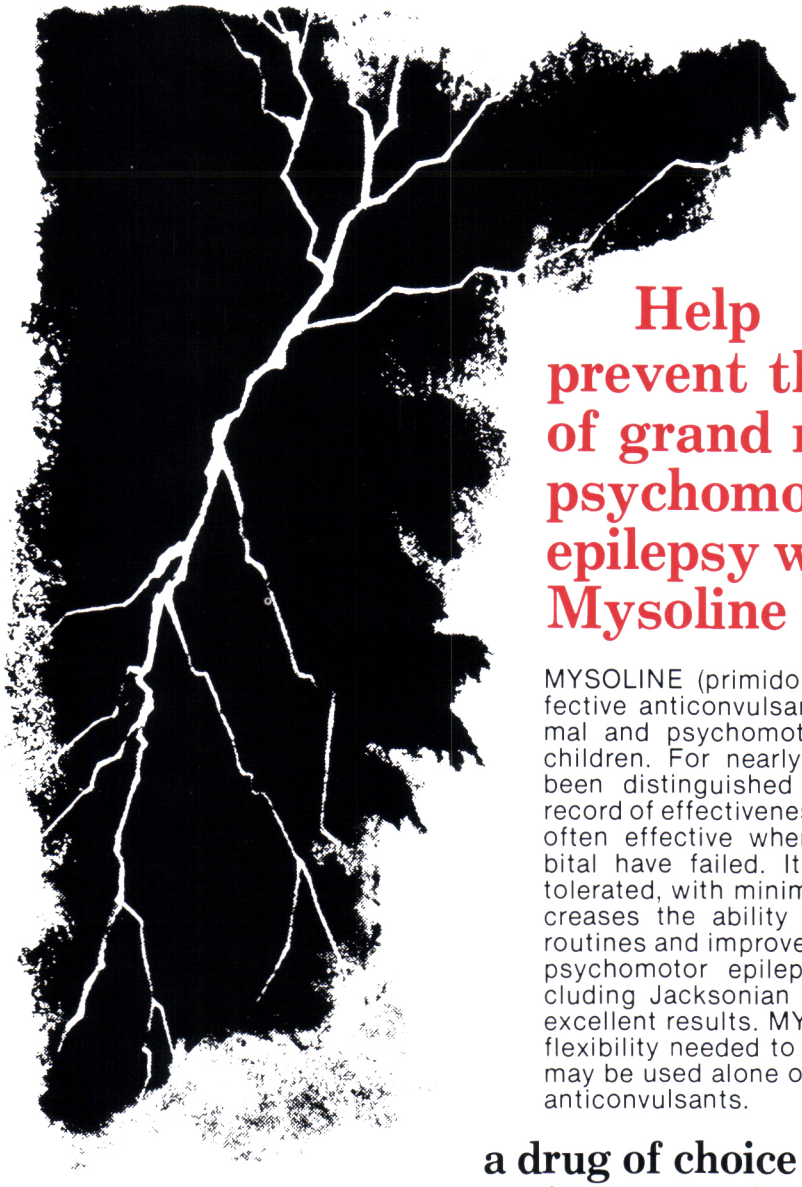

Help prevent the storm of grand mal and psychomotor epilepsy with Mysoline

MYSOLINE (primidone USP) is a safe and effective anticonvulsant for the control of grand mal and psychomotor epilepsy in adults and children. For nearly 20 years MYSOLINE has been distinguished by its worldwide clinical record of effectiveness and safety. MYSOLINE is often effective where phenytoin or phenobarbital have failed. It is also frequently better tolerated, with minimal sedation. MYSOLINE increases the ability to carry out normal daily routines and improves outlook. In grand mal and psychomotor epilepsy, in focal epilepsy, including Jacksonian seizures, MYSOLINE gives excellent results. MYSOLINE allows the dosage flexibility needed to individualize therapy and it may be used alone or in combination with other anticonvulsants.

a drug of choice for control and maintenance in epilepsy.

Mysoline*

Dosage: Adults and children over 8 years—week 1: 250 mg h.s.: week II: 250 mg b.i.d.: week III: 250 mg t.i.d.: week IV: 250 mg q.i.d. Dosage may be increased until seizures are controlled but should not exceed 2 gm daily. Children under 8 years—half the adult dosage. In patients already receiving other anticonvulsants, dosage is gradually increased while the dosage of the other drug(s) is gradually decreased. **Adverse Effects:** Drowsiness, ataxia, vertigo, anorexia, irritability, general malaise, nausea and vomiting. These reactions are usually minor and transitory tending to disappear as therapy is continued or dosage is adjusted. No serious irreversible toxic reactions have been observed. (Occasionally, megaloblastic anemia has been reported, which is reversible by folic acid, 15 mg daily, while MYSOLINE is continued). As with any drug used over prolonged periods, routine laboratory studies at regular intervals are recommended. **Supplied:** Tablets—250 mg and 125 mg Suspension—250 mg/5ml. Complete prescribing information available on request.

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