

THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES

LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

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Official Journal of
The Canadian Neurological Society
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REFERENCES:

- 1 Frew, I.J.C. et al: Postgrad. Med. J.; 52:501-503, 1976.
2 Wilmot, T.J. et al: J. Laryng. Otol; 9:833-840, 1976.

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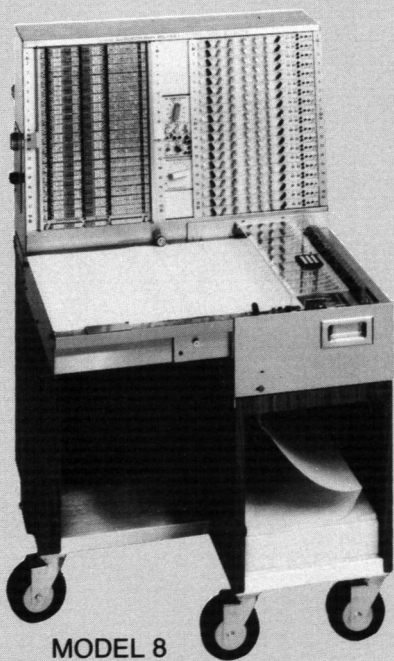
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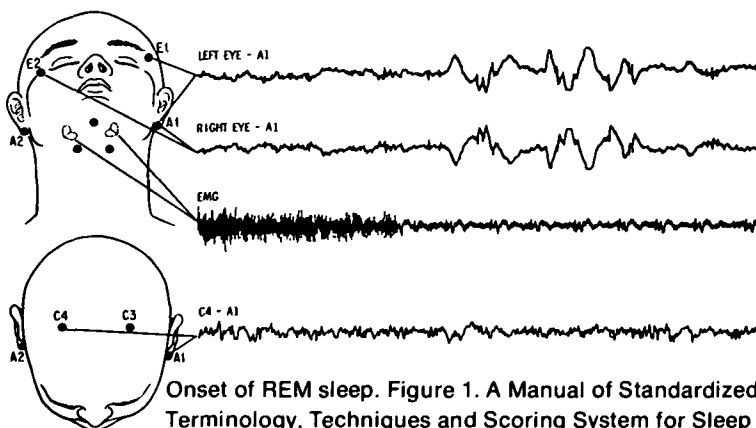
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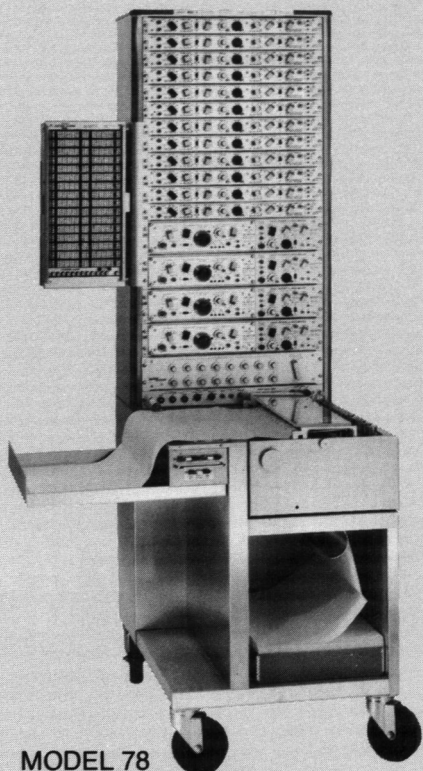


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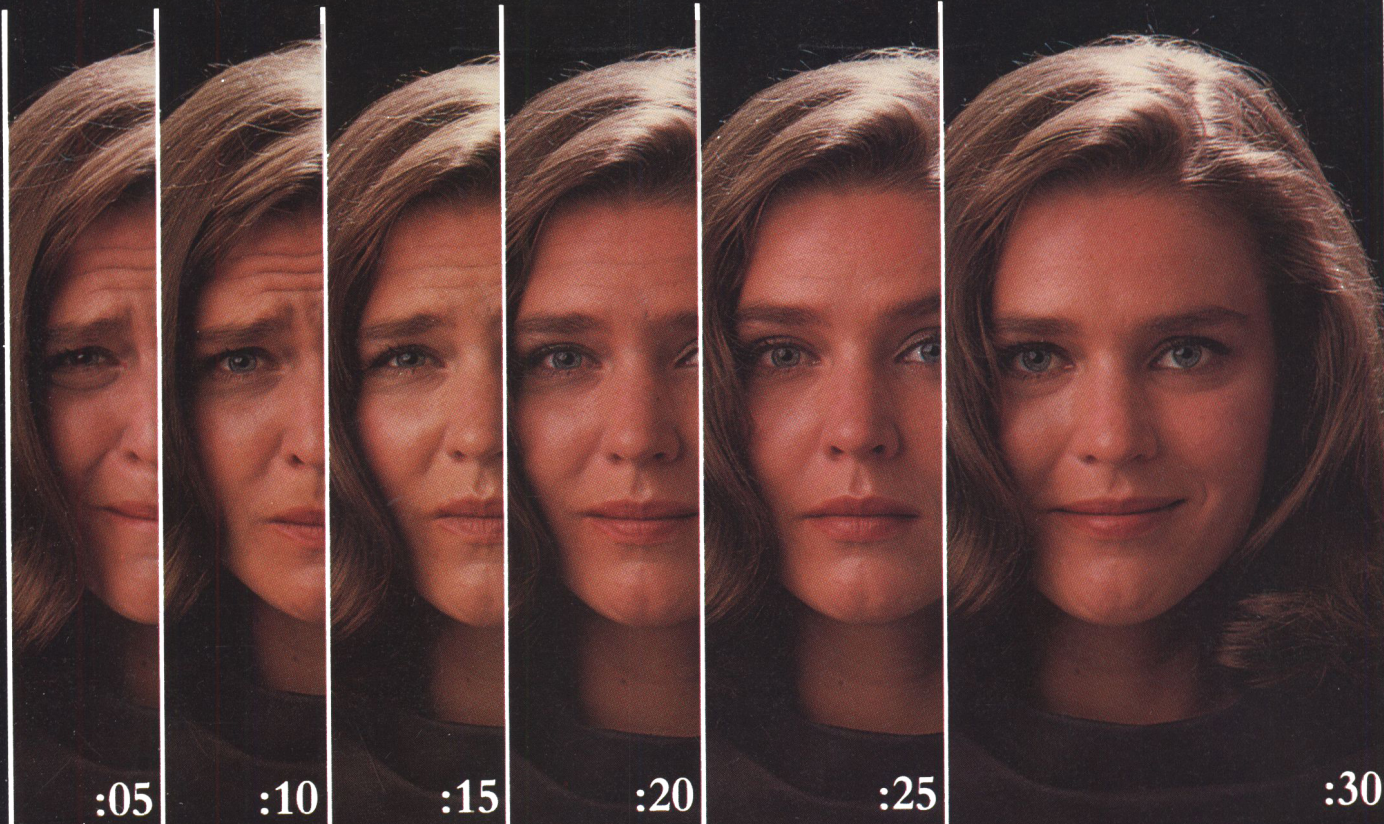
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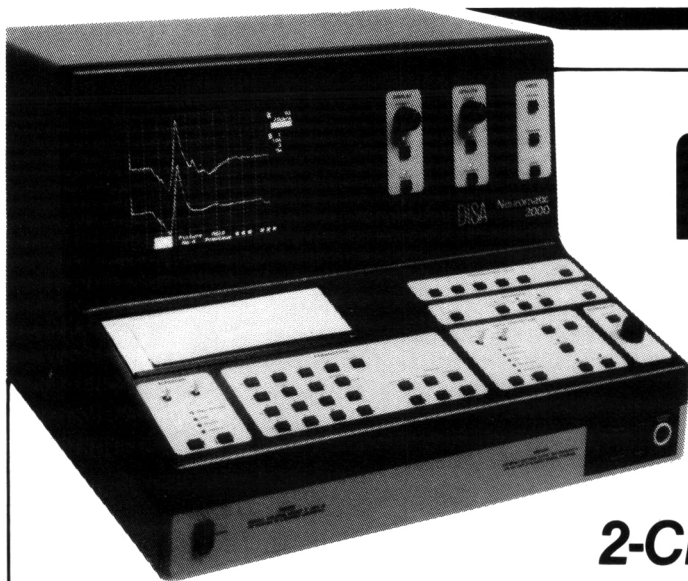
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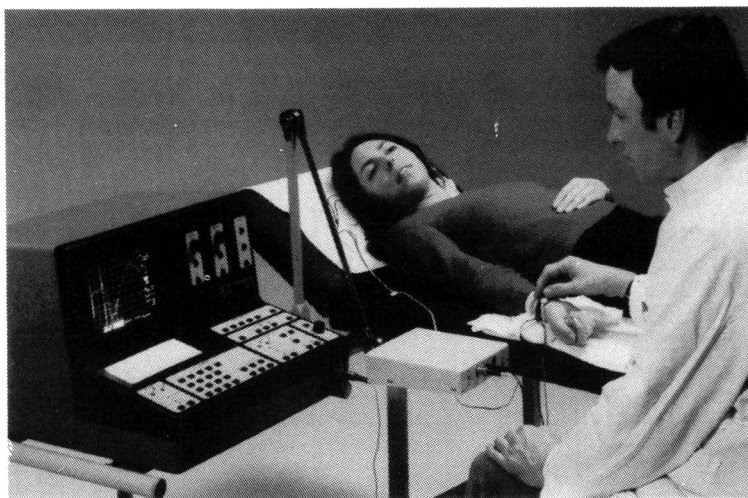
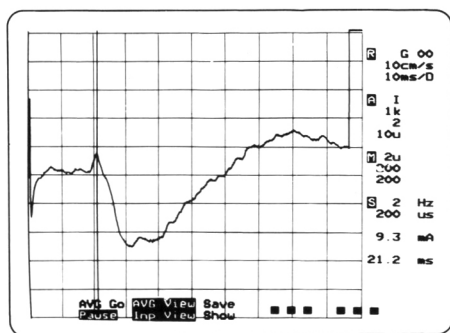
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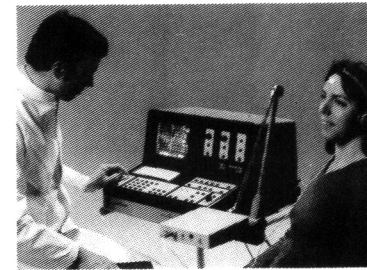
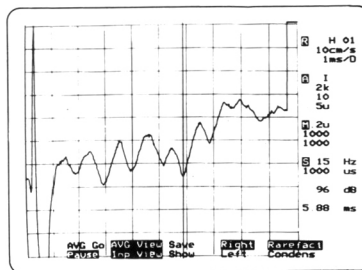
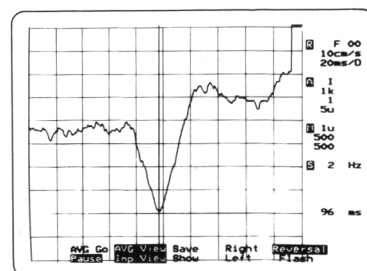
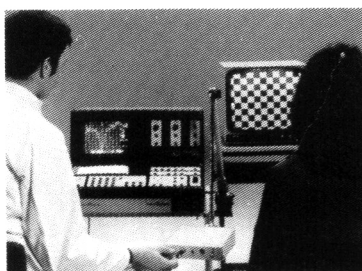
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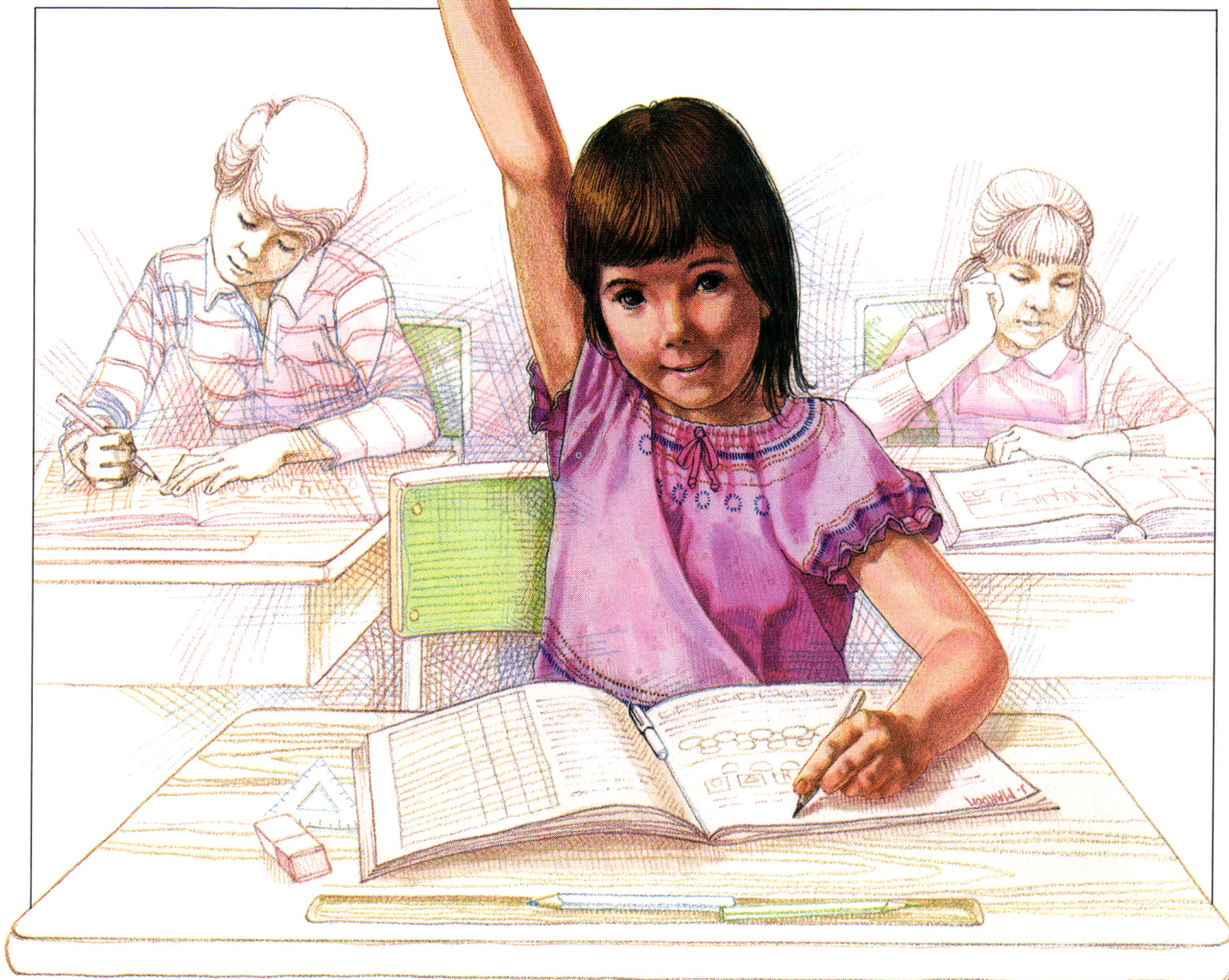
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Minimizes problems of polypharmacy Depakene is often effective as single therapy. When other anticonvulsants are necessary, their dosage may be reduced.

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Prescribing information on page...

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valproic acid

Brief prescribing information

INDICATIONS AND CLINICAL USE: Depakene (valproic acid) is indicated for use as sole and adjunctive therapy in the treatment of simple and complex absence seizures, including petit mal. Valproic acid may also be used adjunctively in patients with multiple-seizure types which include absence.

In accordance with the International Classification of Seizures, simple absence is defined as a very brief clouding of the sensorium or loss of consciousness (lasting usually 2-15 seconds), accompanied by certain generalized epileptic discharges without other detectable clinical signs. Complex absence is the term used when other signs are also present.

CONTRAINDICATIONS: Depakene (valproic acid) should not be administered to patients with hepatic disease or significant dysfunction; it is contraindicated in patients with known hypersensitivity to the drug.

WARNINGS: Hepatic failure resulting in fatalities has occurred in patients receiving Depakene. These incidences usually have occurred during the first six months of treatment with Depakene. Serious or fatal hepatotoxicity may be preceded by non-specific symptoms such as loss of seizure control, malaise, weakness, lethargy, anorexia and vomiting. Patients and parents should be instructed to report such symptoms. Because of the nonspecific nature of some of the early signs, hepatotoxicity should be suspected in patients who become unwell, other than through obvious causes while taking sodium valproate. Liver function tests should be performed prior to therapy and at frequent intervals thereafter especially during the first six months. However, physicians should not rely totally on serum biochemistry since these tests may not be abnormal in all instances, but should also consider the results of careful interim medical history and physical examination. Caution should be observed when administering Depakene to patients with a prior history of hepatic disease. Patients with various unusual congenital disorders, those with severe seizure disorders accompanied by mental retardation, and those with organic brain disease may be at particular risk.

In high-risk patients, it might also be useful to monitor serum fibrinogen and albumin for decrease in concentrations and serum ammonia for increases in concentration. If changes occur, valproic acid should be discontinued. Dosage should be titrated to and maintained at the lowest dose consistent with optimal seizure control.

The drug should be discontinued immediately in the presence of significant hepatic dysfunctions, suspected or apparent. In some cases, hepatic dysfunction has progressed in spite of discontinuation of drug. The frequency of adverse effects particularly elevated liver enzymes may increase with increasing dose. Therefore, the benefit gained by increased seizure control by increasing the dosage must be weighed against the increased incidence of adverse effects sometimes seen at higher dosages.

USE IN PREGNANCY: The safety of Depakene (valproic acid) during pregnancy has not been established, however, animal studies have demonstrated teratogenicity. Therefore, the physician should weigh the potential benefits against the possible risks in treating or counselling women of childbearing age who have epilepsy. Recent reports indicate an association between the use of anticonvulsant drugs and an elevated incidence of birth defects in children born to epileptic women taking such medication during pregnancy. The incidence of congenital malformations in the general population is regarded to be approximately 2%; in children of treated epileptic women, this incidence may be increased two to three-fold. The increase is largely due to specific defects, e.g. congenital malformations of the heart, and cleft lip and/or palate. Nevertheless, the great majority of mothers receiving anticonvulsant medications deliver normal infants.

Data are more extensive with respect to diphenylhydantoin and phenobarbital, but these drugs are also the most commonly prescribed anticonvulsants. Some reports indicate a possible similar association with the use of other anticonvulsant drugs, including trimethadione and paramethadione. However, the possibility also exists that other factors, e.g. genetic predisposition or the epileptic condition itself may contribute to or may be mainly responsible for the higher incidence of birth defects.

Anticonvulsant drugs should not be discontinued in patients to whom the drug is administered to prevent major seizures, because of the strong possibility of precipitating status epilepticus with attendant hypoxia and risks to both the mother and the unborn child. With regard to drugs given for minor seizures, the risks of discontinuing medication prior to or during pregnancy should be weighed against the risk of congenital defects in the particular case and with the particular family history.

Epileptic women of child-bearing age should be encouraged to seek the counsel of their physician and should report the onset of pregnancy promptly to him. Where the necessity for continued use of antiepileptic medication is in doubt, appropriate consultation might be indicated.

NURSING MOTHERS: Depakene is secreted in breast milk. Concentrations in breast milk have been reported to be 1 to 10% of serum concentrations. As a general rule, nursing should not be undertaken while a patient is receiving valproic acid.

FERTILITY: Chronic toxicity studies in juvenile and adult rats and dogs demonstrated reduced spermatogenesis and testicular atrophy at doses greater than 200 mg/kg/day in rats and 90 mg/kg/day in dogs. Segment I fertility studies in rats have shown that doses up to 350 mg/kg/day for 60 days have no effect on fertility. The effect of Depakene (valproic acid) on the development of the testes and on sperm production and fertility in humans is unknown.

LONG TERM TOXICITY STUDIES IN RATS INDICATED A POTENTIAL

CARCINOGENIC RISK.

PRECAUTIONS: HEPATIC DYSFUNCTION: SEE CONTRAINDICATIONS AND WARNINGS

GENERAL: Because of reports of thrombocytopenia and platelet aggregation dysfunction, platelet counts and bleeding-time determination are recommended before instituting therapy and at periodic intervals. It is recommended that patients receiving Depakene (valproic acid) be monitored for platelet count prior to planned surgery. Clinical evidence of hemorrhage, bruising or a disorder of hemostasis/coagulation is an indication for reduction of Depakene (valproic acid) dosage or withdrawal of therapy pending investigation.

Hyperammonemia with or without lethargy or coma has been reported and may be present in the absence of abnormal liver function tests; if elevation occurs, the valproic acid should be discontinued.

Because Depakene (valproic acid) may interact with other anticonvulsant drugs, periodic serum level determinations of such other anticonvulsants are recommended during the early part of therapy (see DRUG INTERACTIONS). There have been reports of breakthrough seizures occurring with the combination of Depakene and phenytoin. Depakene (valproic acid) is partially eliminated in the urine as a ketone-containing metabolite which may lead to a false interpretation of the urine ketone test.

DRIVING AND HAZARDOUS OCCUPATIONS: Valproic acid may produce CNS depression, especially when combined with another CNS depressant, such as alcohol. Therefore, patients should be advised not to engage in hazardous occupations, such as driving a car or operating dangerous machinery, until it is known that they do not become drowsy from the drug.

DRUG INTERACTIONS: DEPAKENE (VALPROIC ACID) MAY POTENTIATE THE CNS DEPRESSANT ACTION OF ALCOHOL.

THERE IS EVIDENCE THAT VALPROIC ACID MAY CAUSE AN INCREASE IN SERUM PHENOBARBITAL LEVELS, ALTHOUGH THE MECHANISM IS UNKNOWN. PATIENTS RECEIVING CONCOMITANT BARBITURATE THERAPY SHOULD BE CLOSELY MONITORED FOR NEUROLOGICAL TOXICITY. SERUM BARBITURATE DRUG LEVELS SHOULD BE OBTAINED, IF POSSIBLE, AND THE BARBITURATE DOSAGE DECREASED, IF INDICATED.

Primidone is metabolized into a barbiturate, and therefore, may also be involved in a similar or identical interaction.

THERE IS CONFLICTING EVIDENCE REGARDING THE INTERACTION OF VALPROIC ACID WITH PHENYTOIN. IT IS NOT KNOWN IF THERE IS A CHANGE IN UNBOUND (FREE) PHENYTOIN SERUM LEVELS. THE DOSE OF PHENYTOIN SHOULD BE ADJUSTED AS REQUIRED BY THE CLINICAL SITUATION. THE CONCOMITANT USE OF VALPROIC ACID AND CLONAZEPAM MAY PRODUCE ABSENCE STATUS.

Caution is recommended when valproic acid is administered with drugs affecting coagulation, e.g. acetylsalicylic acid and warfarin (see ADVERSE REACTIONS).

ADVERSE REACTIONS: The most commonly reported adverse reactions are nausea, vomiting and indigestion. Since Depakene (valproic acid) has usually been used with other anticonvulsants, it is not possible in most cases to determine whether the adverse reactions mentioned in this section are due to valproic acid alone or to the combination of drugs.

GASTROINTESTINAL: Nausea, vomiting and indigestion are the most commonly reported side effects at the initiation of therapy. These effects are usually transient and rarely require discontinuation of therapy. Diarrhea, abdominal cramps and constipation have also been reported. Anorexia with some weight loss and increased appetite with some weight gain have also been seen.

CNS EFFECTS: Sedative effects have been noted in patients receiving valproic acid alone but are found most often in patients on combination therapy. Sedation usually disappears upon reduction of other anticonvulsant medication. Ataxia, headache, nystagmus, diplopia, asterix, "spots before the eyes", tremor, dysarthria, dizziness, and incoordination have rarely been noted. Rare cases of coma have been reported in patients who were also on phenobarbital.

DERMATOLOGIC: Transient increases in hair loss have been observed. Skin rash and petechiae have rarely been noted.

ENDOCRINE: There have been reports of irregular menses and secondary amenorrhea in patients receiving Depakene.

PSYCHIATRIC: Emotional upset, depression, psychosis, aggression, hyperactivity and behavioural deterioration have been reported.

MUSCULOSKELETAL: Weakness has been reported.

HEMATOPOIETIC: Thrombocytopenia has been reported. Valproic acid inhibits the second phase of platelet aggregation (see DRUG INTERACTIONS). This may be reflected in altered bleeding time. Bruising, hematoma formation and frank hemorrhage have been reported. Relative lymphocytosis and hypofibrinogenemia have been noted. Leukopenia and eosinophilia have also been reported.

HEPATIC: Minor elevations of transaminases (e.g. SGOT and SGPT) and LDH are frequent and appear to be dose-related. Occasionally, laboratory tests also show increases in serum bilirubin and abnormal changes in other liver function tests. These results may reflect potentially serious hepatotoxicity. (See WARNINGS).

METABOLIC: Hyperammonemia. (See PRECAUTIONS). Hyperglycemia has been reported and associated with a fatal outcome in a patient with pre-existing nonketotic hyperglycemia.

PANCREATIC: Isolated reports of pancreatitis in association with valproic acid therapy have been received.

SYMPTOMS AND TREATMENT OF OVERDOSAGE: In a reported case of overdose with Depakene (valproic acid) after ingesting 36 g in combination with phenobarbital and phenytoin, the patient presented in deep coma. An EEG recorded diffuse slowing, compatible with the state of consciousness. The patient made an uneventful recovery. Naloxone has been reported to reverse the CNS depressant effects of Depakene overdose. Because naloxone could theoretically also reverse the anticonvulsant effects of Depakene it should be used with caution.

As valproic acid is absorbed very rapidly, gastric lavage may be of limited value. General supportive measures should be applied with particular attention to the prevention of hypovolemia and the maintenance of adequate urinary output.

DOSAGE AND ADMINISTRATION: Depakene (valproic acid) is administered orally. The recommended initial dose is 15 mg/kg/day, increasing at one-week intervals by 5 to 10 mg/kg/day until seizures are controlled or side effects preclude further increases.

The maximal recommended dose is 60 mg/kg/day. When the total daily dose exceeds 250 mg, it is given in a divided regimen. A 500-mg enteric coated capsule may be substituted for two 250-mg capsules.

The frequency of adverse effects (particularly elevated liver enzymes) may increase with increasing dose. Therefore, the benefit gained by increased seizure control must be weighed against the increased incidence of adverse effects.

Table of Initial Doses by Weight (based on 15 mg/kg/day)

kg	Weight	lb	Total Daily Dose (mg)	Number of Capsules or Teaspoonfuls of Syrup		
				Dose 1	Dose 2	Dose 3
10 - 24.9		22 - 54.9	250	0	0	1
25 - 39.9		55 - 87.9	500	1	0	1
40 - 59.9		88 - 131.9	750	1	1	1
60 - 74.9		132 - 164.9	1,000	1	1	2
75 - 89.9		165 - 197.9	1,250	2	1	2

As the dosage of valproic acid is raised, blood levels of phenobarbital and/or phenytoin may be affected (see PRECAUTIONS).

Patients who experience G.I. irritation may benefit from administration of the drug with food or by a progressive increase of the dose from an initial low level. Such patients may benefit from administration of the enteric-coated capsule. The capsules should be swallowed without chewing to avoid local irritation of the mouth and throat.

AVAILABILITY: Depakene (valproic acid) is available as orange-coloured, soft-gelatin capsules of 250 mg in bottles of 100 capsules (Number 5681; DIN 443840); pale yellow, oval soft gelatin enteric-coated capsules of 500 mg in bottles of 100 capsules (Number D795; DIN 507989) and as a red syrup containing the equivalent of 250 mg valproic acid, as the sodium salt, per 5 mL in bottles of 450 mL (Number 5682; DIN 443832).

Depakene is now available in a 500-mg enteric-coated capsule.

REFERENCES:

1. BMJ editorial, March 3, 1979.
2. Data on file, Abbott Laboratories.
3. Jeavons PM et al: Treatment of generalized epilepsies of childhood and adolescence with sodium valproate. Dev Med Child Neurol 1977; 19: 9-25.
4. Wilder BJ: Valproic acid in clinical use: An overview. Proceedings of the Valproic Acid Round Table Conference, June 1978, Vancouver. Excerpta Medica 1979.
5. Coulter DL et al: Valproic acid in childhood epilepsy. JAMA 1980; 244 (8): 785-88.

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The brochure on the WILD M 600 Series Surgical Operating Microscopes is available on request, and describes in detail the possibilities of this new line.



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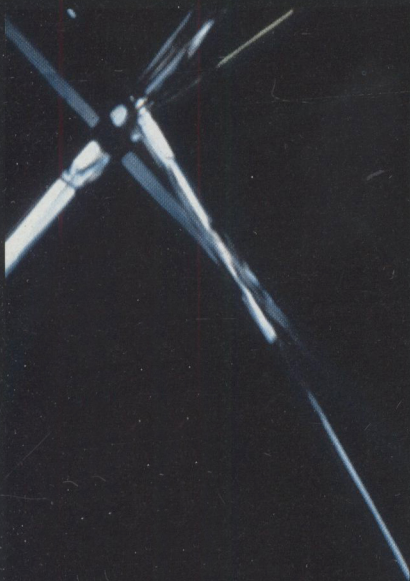
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DILANTIN*

Extended Phenytoin Sodium Capsules U.S.P. A RECOGNIZED DIFFERENCE



USP XX now differentiates between Extended and Prompt Phenytoin Sodium Capsules.

Extended phenytoin sodium has been recognized as a distinct pharmaceutical entity. Its slow dissolution and absorption do not create significant fluctuations in phenytoin blood levels.

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DILANTIN Capsules have not changed.

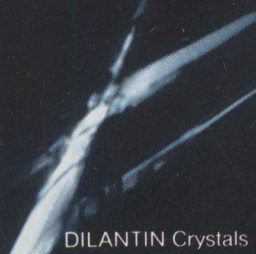
Extended effect has always been the action of DILANTIN therapy. Only the U.S.P. standards have changed to recognize the difference between "extended"

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Extended action of DILANTIN offers greater **convenience and improved patient compliance**. Dependable, effective therapy is

now available through a once-daily-dosage option, once seizure control has been established with divided doses.



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DILANTIN formulation ensures dependable bioavailability.

Extended phenytoin classification of DILANTIN capsules is the result of its unique dissolution profile. Due to its **special**

formulation, DILANTIN exerts a slow, steady release of phenytoin for **dependable bioavailability**.

**Patients should be maintained on one form of phenytoin (extended or prompt) to avoid toxicity or loss of seizure control.

**START WITH DILANTIN—STAY WITH DILANTIN
FOR OVER A GENERATION,
THE STANDARD IN EPILEPSY MANAGEMENT**

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Parke Davis Canada Inc. Scarborough, Ontario



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This logo appearing on pharmaceutical advertisements in professional journals means that the advertisements have been reviewed—and cleared for publishing—by the Pharmaceutical Advertising Advisory Board/Conseil Consultatif de Publicité Pharmaceutique.

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BRIEF PRESCRIBING INFORMATION DILANTIN*

Extended Phenytoin
Sodium Capsules, U.S.P.
100 mg
ANTICONVULSANT

INDICATIONS

Dilantin is indicated for the control of generalized tonic-clonic (grand mal) seizures and complex partial (psychomotor) seizures.

CONTRAINDICATIONS

Dilantin is contraindicated in those patients with a history of hypersensitivity to hydantoin products.

WARNINGS

Abrupt withdrawal of phenytoin in epileptic patients may precipitate status epilepticus. Phenytoin is not indicated in seizures due to hypoglycemia or other causes which may be immediately identified and corrected.

Phenytoin metabolism may be significantly altered by the concomitant use of other drugs such as:

A Barbiturates may enhance the rate of metabolism of phenytoin. This effect, however, is variable and unpredictable. It has been reported that in some patients the concomitant administration of carbamazepine resulted in an increased rate of phenytoin metabolism.

B Coumarin anticoagulants, disulfiram, phenylbutazone, and sulfaphenazole may inhibit the metabolism of phenytoin, resulting in increased serum levels of the drug. This may lead to an increased incidence of nystagmus, ataxia, or other toxic signs.

C Isoniazid inhibits the metabolism of phenytoin so that with combined therapy, patients who are slow acetylators may suffer from

phenytoin intoxication.

D Tricyclic antidepressants in high doses may precipitate seizures, and the dosage of phenytoin may have to be adjusted accordingly.

Usage in Pregnancy: The effects of Dilantin in human pregnancy and nursing infants are unknown.

The prescribing physician will have to determine the risk/benefit in treating or counselling epileptic women of childbearing potential.

PRECAUTIONS

The liver is the chief site of biotransformation of phenytoin, patients with impaired liver function may show early signs of toxicity. Elderly patients or those who are gravely ill may show early signs of toxicity.

A small percentage of individuals who have been treated with phenytoin have been shown to metabolize the drug slowly. Slow metabolism may be due to limited enzyme availability and lack of induction; it appears to be genetically determined.

Phenytoin has been associated with reversible lymph node hyperplasia. If lymph node enlargement occurs in patients on phenytoin, every effort should be made to substitute another anticonvulsant drug or drug combination.

Drugs that control generalized tonic-clonic (grand mal) seizures are not effective for absence (petit mal) seizures. Therefore, if both conditions are present, combined drug therapy is needed.

Hyperglycemia, resulting from the drug's inhibitory effect on insulin release, has been reported. Phenytoin may also raise the blood sugar level in persons already suffering from hyperglycemia.

ADVERSE REACTIONS

Central Nervous System: The most common manifestations encountered with phenytoin

therapy include nystagmus, ataxia, slurred speech, and mental confusion. Dizziness, insomnia, transient nervousness, motor twitchings, and headache have also been observed. These side effects may disappear with continuing therapy at a reduced dosage level.

Gastrointestinal System: Phenytoin may cause nausea, vomiting, and constipation. Administration of the drug with or immediately after meals may help prevent gastrointestinal discomfort.

Integumentary System: Dermatological manifestations sometimes accompanied by fever have included scarlatiniform or morbilliform rashes.

Hemopoietic System: Hemopoietic complications, some fatal, have occasionally been reported in association with administration of phenytoin. These have included thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, and pancytopenia.

Other: Gingival hyperplasia occurs frequently; this incidence may be reduced by good oral hygiene including gum massage, frequent brushing and appropriate dental care. Polyarthropathy and hirsutism occur occasionally. Hyperglycemia has been reported. Toxic hepatitis, liver damage, and periarteritis nodosa may occur and can be fatal.

MANAGEMENT OF OVERDOSAGE

The mean lethal dose in adults is estimated to be 2 to 5 grams. The cardinal initial symptoms are hystagmus, ataxia and dysarthria. The patient then becomes comatose, the pupils are unresponsive and hypotension occurs. Death is due to respiratory depression and apnea. Treatment is non-specific since there is no known antidote. First, the stomach should be emptied. If the gag reflex is absent, the airway should be supported. Oxygen, vasopressors and assisted ventilation may be necessary for central nervous system, respiratory and

cardiovascular depression. Finally, hemodialysis can be considered since phenytoin is not completely bound to plasma proteins.

DOSAGE AND ADMINISTRATION

Dosage should be individualized to provide maximum benefit. In some cases, serum blood level determinations may be necessary for optimal dosage adjustments—the clinically effective serum level is usually 10–20 mcg/mL.

Adult Dose: Patients who have received no previous treatment may be started on one 100 mg Dilantin Capsule three times daily, and the dose then adjusted to suit individual requirements.

Pediatric Dose: Initially, 5 mg/kg/day in two or three equally divided doses, with subsequent dosage individualized to a maximum of 300 mg daily. A recommended daily maintenance dosage is usually 4 to 8 mg/kg. Children over 6 years old may require the minimum adult dose (300 mg/day). Pediatric dosage forms available include a 30 mg Capsule, a 50 mg palatable flavoured Infatab, or an oral suspension form containing 30 mg of Dilantin in each 5 mL.

Alternative Dose: Once-a-day dosage for adults with 300 mg of Dilantin may be considered if seizure control is established with divided doses of three 100 mg Capsules daily.

HOW SUPPLIED

Dilantin 100 mg Capsules; in bottles of 100 & 1000.

Complete prescribing information available upon request.

PARKE-DAVIS

Parke-Davis Canada Inc., Scarborough, Ontario

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In the effective treatment of epilepsy, there is no substitute for experience.

The original carbamazepine, TEGRETOL[®], was first introduced by Geigy in 1969 and subsequently became the drug of choice for trigeminal neuralgia.

But this development marked only the beginning.

Geigy research soon provided the basis for approval in the treatment of psychomotor/temporal lobe epilepsy in 1973.

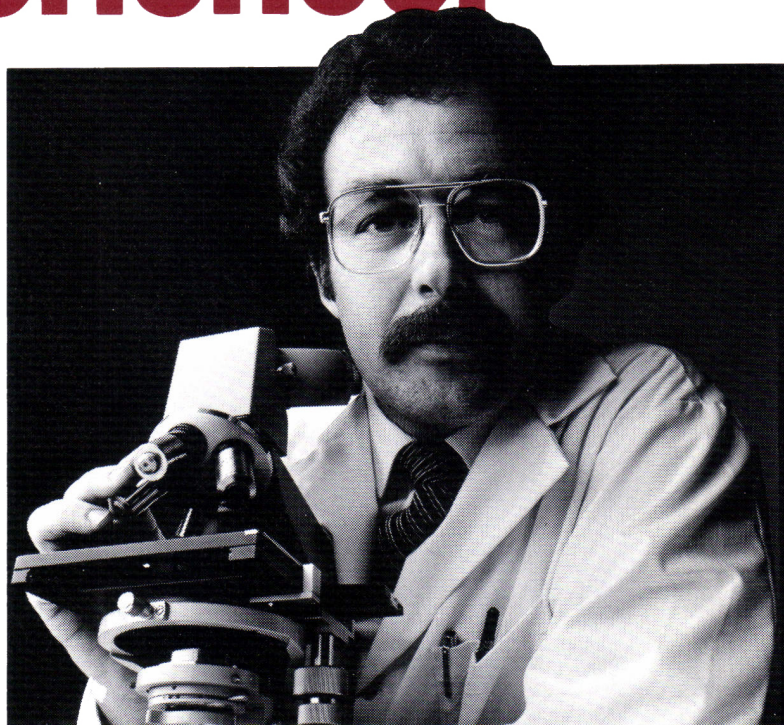
And in 1979, this indication was again expanded to include usage in refractory generalized tonic/clonic seizures.

This commitment to the ongoing potential of TEGRETOL does not end here: continuing research indicates that further applications are possible in the future.

While the provision of a quality pharmaceutical is a primary objective of Geigy, other services to both doctor and patient have not gone unaddressed.

Medical information, support to continuing medical education and attention to the needs of epileptic patients, their families and Associations have been important elements in the overall attention given to this disorder.

In fact, a prescription for TEGRETOL does far more in the fight against epilepsy than just control patient symptoms.



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No Substitution.
Because there is
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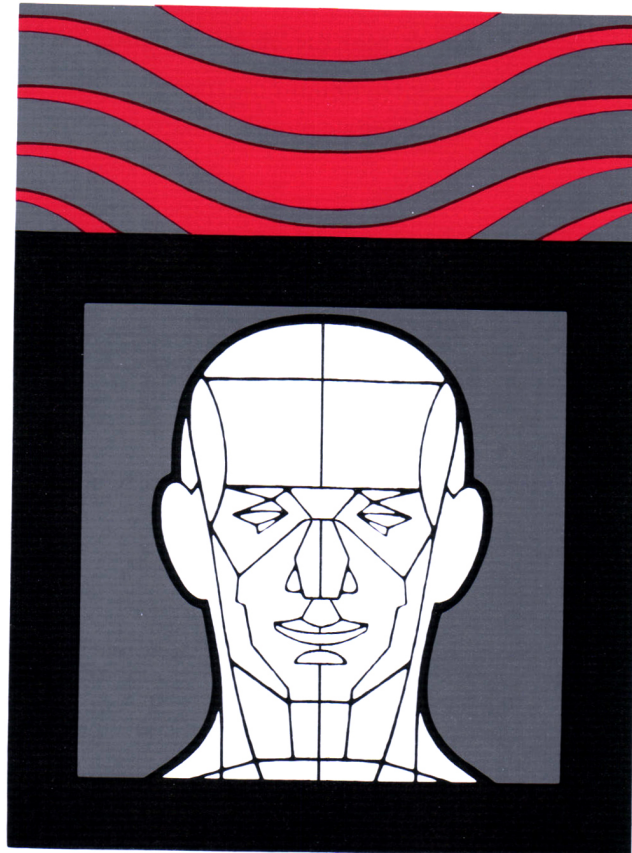
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Help prevent recurrent throbbing headaches with **Sandomigran DS** (double strength)

1 mg
tablet
double strength



Sandomigran maintenance therapy helps prevent recurrent headaches

Taken daily, Sandomigran can reduce the frequency, severity and duration of vascular or mixed headaches.¹⁻³ In fact, Sandomigran has suppressed throbbing headaches altogether in many patients.³⁻⁵

Double-strength DS tablet improves compliance

Patients have fewer tablets to take and find it easier to comply with maintenance therapy. The DS tablet also simplifies dosage: with a half-life of 23 hours,⁶ treatment can be initiated h.s.; the dosage may be increased to a maximum of 6 DS tablets a day in divided doses (see prescribing information).

Sandomigran DS for at least 4 weeks

Sandomigran DS must be taken daily for at least four weeks — not to relieve headaches but to prevent them.

Sandomigran® DS 1 mg pizotyline

Doesn't give recurrent throbbing headaches a second chance.



Dosage information page



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THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

with the co-operation of the Canadian Neurosurgical Society
announces

THE K.G. MCKENZIE MEMORIAL AWARDS

to honour the memory of
Canada's pioneer neurosurgeon

AWARD 1. A citation and prize of \$100.00 will be awarded for the best paper presented to the annual meeting of the Canadian Neurosurgical Society by a neurosurgical resident in which he is the principal author. The recipient, as well, will have his expenses, including Air Fare, Hotel Accommodation and Registration Fees, paid for as part of the Award.

AWARD 2. A grant-in-aid will be awarded to support a specific educational project which may include travel. (However, travel to regularly scheduled neurosurgical meetings is excluded.) The applicant must be a resident in training in a Canadian Neurosurgical Training Program, or if formal training is completed, within two years of having received certification in neurosurgery.

APPLICATIONS FOR AWARD 1.

Papers should be received by the chairman of the Awards Committee not later than January 15. All papers received will be automatically forwarded to the program chairman for the annual meeting of the Canadian Congress of Neurological Sciences for further consideration. The successful candidate will be notified by April 1, and the awards will be presented at the annual meeting in June.

APPLICATIONS FOR AWARD 2.

Applicants should forward a comprehensive letter to the chairman of the Awards Committee by January 15. The application should contain relevant personal information, a clear description of the educational project which is contemplated; and its purpose, and any supporting letters the applicant may wish to submit. The successful applicant will be notified by April 1.

APPLICATIONS SHOULD BE SENT TO:

Chairman
K.G. McKenzie Memorial Awards Committee
Room 2 — 113 Centennial Wing, Victoria General Hospital
HALIFAX, Nova Scotia

THE FRANCIS McNAUGHTON AWARD

The Francis McNaughton Award is awarded by the Canadian Neurological Society for the best paper submitted to the Canadian Congress of Neurological Sciences by a junior member of the society or a resident in a neurology training program. Full members of the society who have completed their clinical training and obtained certification in neurology within the past two years are also eligible to apply.

The work should be original and should not have been presented previously. Applicants need not be the sole author but should be primarily responsible for the work to be presented.

The award includes an honorarium of \$200, return air fare to the city of the congress and a suitably inscribed book prize.

In addition to the regular abstract for the congress, applicants should submit in triplicate an expanded abstract of approximately 2,000 words.

Applications should be submitted to:

Dr. William Pryse-Phillips
Health Sciences Centre
St. John's, Newfoundland
A1B 3V6

Deadline: February 15, 1983

THE JASPER PRIZE IN CLINICAL NEUROPHYSIOLOGY

The Jasper Prize is awarded by the Canadian Society of Clinical Neurophysiologists for the best original work based on clinical neurophysiology done by a resident or post-doctoral fellow.

The prize consists of an honorarium of \$100 plus return air fare to the congress.

Applications should be submitted to:

Dr. William Pryse-Phillips
Health Sciences Centre
St. John's, Newfoundland
A1B 3V6

Deadline: February 15, 1983.