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Depakene*

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, asterixis, "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). Hyperglycinemia has been reported and associated with a fatal outcome in a patient with pre-existing nonketotic hyperglycinemia.

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

SYMPTOMS AND TREATMENT OF OVERDOSAGE: In a reported case of overdosage 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)

Weight		Total Daily Dose (mg)	Number of Capsules or Teaspoonfuls of Syrup		
kg	lb		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.

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4. Wilder BJ: Valproic acid in clinical use: An overview. Proceedings of the Valproic Acid Round Table Conference, June 1978, Vancouver. Excerpta Medica 1979.
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PHARMACEUTICAL PRODUCTS DIVISION
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HEXADROL*

Adrenocortical Steroid

(dexamethasone sodium phosphate injection U.S.P.)

PRESCRIBING INFORMATION

ACTIONS: Dexamethasone Sodium Phosphate is a synthetic analogue of the naturally-occurring glucocorticoid, hydrocortisone. Glucocorticoids cause profound and varied metabolic effects and are able to modify the body's immune responses to diverse stimuli. Due to the introduction of a 1, 2 double bond, a methyl group at carbon 16, and a fluoride group at carbon 9, dexamethasone has markedly enhanced anti-inflammatory and significantly diminished sodium-retaining properties.

INDICATIONS: Cerebral edema of diverse etiologies in conjunction with adequate neurological evaluation and management. For a complete list of indications please consult the product monograph.

CONTRAINDICATIONS: Systemic fungal infections; hypersensitivity to any component of the medication.

WARNINGS: In patients on corticosteroid therapy subjected to any unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Corticosteroids may mask some signs of infection and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Corticosteroids should be used cautiously in patients with ocular herpes simplex for fear of corneal ulceration and perforation.

Usage in Pregnancy. Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential, requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and may suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Therefore, mothers taking these drugs should be advised not to breastfeed their babies.

Average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

While on Corticosteroid Therapy Patients Should Not be Vaccinated Against Smallpox. Other Immunization Procedures Should Not be Undertaken in Patients who Are on Corticosteroids, Especially in High Doses, Because of Possible Hazards of Neurological Complications and Lack of Antibody Response.

The use of HEXADROL* Phosphate Injection in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with appropriate anti-tuberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

Idiopathic thrombocytopenic purpura in adults should be treated by intravenous injection.

PRECAUTIONS: Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of the dosage. This type of relative insufficiency may persist for *months after discontinuation of therapy; therefore, in any* situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

When corticosteroids are administered concomitantly with potassium—depleting diuretics, patients should be observed closely for development of hypokalemia.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction must be gradual.

When large doses are given, some authorities advise that antacids be administered between meals to prevent peptic ulcer.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection, also in diverticulitis, fresh intestinal anastomoses, active or latent *peptic ulcer, renal insufficiency, hypertension, osteoporosis* and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully followed.

Intra-articular injection of a corticosteroid may produce systemic as well as local effects.

Frequent intra-articular injection may result in damage to joint tissues.

Patients should be impressed strongly with the importance of not overusing joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

Appropriate examination of any joint fluid present is necessary to exclude a septic process.

A marked increase in pain, accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.

Local injection of a steroid into a previously infected joint is to be avoided. Corticosteroids should not be injected into unstable joints.

Patients who have received prolonged corticoid therapy may develop a state of relative adrenal insufficiency which may persist for a year or more following cessation of therapy.

Psychological and/or physiological dependency may develop with long-term use of corticosteroids. Withdrawal symptoms, including anorexia, vague pains, weakness and lethargy may occur.

It may prove lifesaving in critically ill patients suffering from severe overwhelming infections for which specific antibiotic therapy is available. It may permit survival until the antibiotic has had time to take effect. Since corticoids mask the classical signs of infection, their use in such cases must be undertaken with the greatest caution. Bacteriological studies and adequate antibiotic therapy must be started before the first dose of this corticoid and its use should be discontinued as soon as possible and at least three days before antibiotic therapy is stopped.

Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control drug reactions to amphotericin B. Moreover, there have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive failure.

Diphenylhydantoin, phenobarbital, and ephedrine may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiological activity, thus requiring adjustment in corticosteroid dosage. This interaction may interfere with the dexamethasone suppression test which should be interpreted with caution during administration of these drugs.

The slower rate of absorption by intramuscular injection should be recognized.

Corticosteroids may suppress reactions to skin tests.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect is inhibition of response to coumarins, although there have been conflicting reports of potentiation.

Injection into the deltoid muscle should be avoided because of the high incidence of subcutaneous atrophy.

In intercostal neuritis and neuralgia, guard against entering the pleura.

Overdistention of the joint capsule and deposition of steroid along the needle track should be avoided in intra-articular injection since this may lead to tissue atrophy.

Steroids may increase or decrease motility and number of spermotozoa in some patients.

Patients should be advised to inform any new physician that they have been on corticosteroid therapy.

ADVERSE REACTIONS:
1. Fluid and electrolyte disturbances: sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, hypertension, hypotension or shock-like reaction. **2. Musculoskeletal:** muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathologic fracture of long bones. **3. Gastrointestinal:** peptic ulcer with possible subsequent perforation and hemorrhage, pancreatitis, abdominal distention, ulcerative esophagitis. **4. Dermatologic:** impaired wound healing, thin fragile skin, petechiae and ecchymoses, burning or tingling, especially in the perineal area (after I.V. injection), facial erythema, increased *sweating, may suppress reactions to skin tests,* other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema. **5. Neurological:** increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment, convulsions, vertigo, headache. **6. Endocrine:** menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness, particulary in times of stress, as in trauma, surgery, or illness, decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycemic agents in diabetics. **7. Ophthalmic:** Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos. **8. Metabolic:** Negative nitrogen balance due to protein catabolism. **9. Miscellaneous:** Hyperpigmentation or hypopigmentation, subcutaneous and cutaneous atrophy, sterile abscess, postinjection flare, following intra-articular use, charcot-like arthropathy, rare instances of blindness associated with intralesional therapy around the face and head, anaphylactoid or hypersensitivity reactions, thromboembolism, weight gain, increased appetite, nausea, malaise, psychological and physiological dependency.

SYMPTOMS AND TREATMENT OF OVERDOSAGE: Dexamethasone is unlikely to result in acute toxicity due to overdosage because very large single doses of corticosteroids do not give rise to serious side effects. However, should overdosage occur, there is no known antidote. Gastric lavage should be performed in acute overdose. Therapy is otherwise symptomatic.

DOSAGE AND ADMINISTRATION
A. General principles governing administration: 1. Dosage must be individualized according to the severity of the disease and the response of the patient. (For infants and children, the recommended dosage will have to be reduced, but dosage should be governed by the severity of the condition rather than by strict adherence to the ratio indicated by age or body weight). **2.** Hormone therapy is an adjunct to, and not a replacement for, conventional therapy. **3.** Dosage must be decreased or discontinued gradually when the drug has been administered for more than a few days. **4.** The severity, prognosis and expected duration of the disease and the reaction of the patient to medication are primary factors in determining dosage. **5.** If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued. **6.** Routine laboratory studies such as urinalysis, two-hour postprandial blood sugar, determination of blood pressure and body weight, and a chest x-ray should be made at regular intervals during prolonged therapy. Upper GI x-rays are desirable in patients with an ulcer history or significant dyspepsia.

B. Intravenous or Intramuscular Injection: The usual dose varies from 4 to 20 mg depending on the nature and severity of the disease being treated. Intravenous doses exceeding 8 mg should be given slowly over a period of one minute. The initial dose may be repeated as necessary until the desired response is noted. Maintenance doses average 2 to 4 mg daily. After achieving satisfactory control the patient should be switched to oral therapy as soon as feasible.

In the treatment of unresponsive shock, high pharmacologic doses of glucocorticoids are recommended currently. Various dosage regimens have been suggested by different authors. These include: the use of a single intravenous injection of 1-6 mg/kg body weight; continuous infusion of 3 mg/kg body weight per 24 hours after initial intravenous bolus of 20 mg; and initial intravenous bolus of 40 mg followed by repeated intravenous injections every 2-6 hours while the state of shock persists.

Whenever possible use intravenous route for the initial and for as many subsequent doses as are given while the patient is in shock (because of irregular absorption by other routes in such patients). When the blood pressure responds, use the intramuscular route until oral therapy can be substituted.

For the treatment of cerebral edema in adults an initial intravenous dose of 10 mg is recommended, followed by 4 mg intravenously or intramuscularly every 6 hours until maximum response has been noted. This regimen may then be tapered over several days using either parenteral or oral dexamethasone. Non-operative cases of cerebral edema may require continuous therapy to remain free of symptoms of increased intracranial pressure. The smallest effective dose may be used in children, preferably orally. This may approximate 0.2 mg/kg/24 hours in divided doses.

There is a tendency in current medical practice to use high doses of parenteral dexamethasone in the short-term therapy of selected cases of life-threatening cerebral edema. The following dosage regimens have been suggested by various authors:

Dosage Schedule
Gobiet, et al: Adults:[1] 48 mg as a single dose then 8 mg every 2 hours on days 1 and 3; 4 mg every 2 hours on days 2 and 4; 4 mg every 4 hours on days 5 through 8. All doses are to be given parenterally.
Children:[1] age 10-14 years receive one-half adult dose, age less than 10 years receive one-quarter adult dose.
Faupel, et al: Adults:[2] 100 mg intravenously followed by 100 mg intramuscularly 6 hours later then, 4 mg intramuscularly every 6 hours for 8 days, thereafter taper daily by 4 mg.
Bruce, et al: Adults and Children:[3] 1.5 mg/kg as a loading dose followed by 1.5 mg/kg/day for the first 5 days then taper slowly over the following 5 days and discontinue. All doses are to be given parenterally.

Stability studies of HEXADROL* Phosphate Injection diluted in various intravenous solutions in glass or plastic containers have demonstrated that potency is maintained up to 4 weeks at room temperature.

Patients currently being treated with other glucocorticoids may be conveniently transferred to this agent using the following dosage equivalents:

Dexamethasone—0.75 mg = methylprednisolone and triamcinolone—4.0 mg = prednisone and prednisolone—5 mg = hydrocortisone—20 mg = cortisone—25 mg

SUPPLIED: 5 ml (4 mg/ml) *multiple dose vial* (for subcutaneous, intramuscular, or intravenous injection); 10 ml (10 mg/ml) multiple dose vial (for intravenous or intramuscular injection only).

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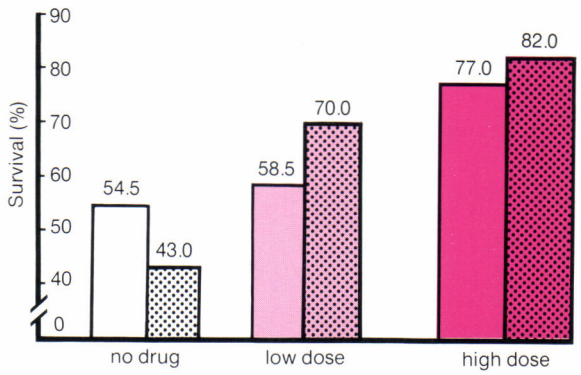
In life-threatening head trauma, survival may be measured in milligrams.

Hexadrol* in high doses increases survival dramatically

While these studies show that even low doses of Hexadrol* will improve the patient's chance for survival, high doses given quickly are much more beneficial.

Survival rates at increasing dosages of dexamethasone in 2 separate studies



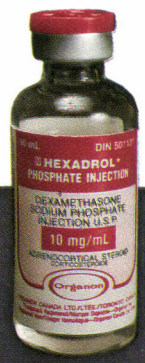
Adapted from:

1. Gobiet W et al: Intracranial Pressure III. Edited by Beks JWF et al, Berlin, Springer-Verlag, 1976 pp. 231-4.
2. Faupel G et al: Dynamics of Brain Edema. Edited by Pappus HM, Feindel W, New York, Springer-Verlag, 1976 pp. 337-43.

	Low Dose	High Dose
Gobiet	16 mg STAT 4 mg q6h	48 mg STAT 8 mg q2h (days 1&3) 4 mg q2h (days 2&4) 4 mg q4h (days 5-8)
Faupel	12 mg STAT 4 mg q6h	100 mg STAT 100 mg (after 6 h) 4 mg q6h

Hexadrol* can be given quickly in high doses

One 10 mL vial contains 100 mg — enough to initiate therapy in these life-threatening cases. Hexadrol* is already in solution. No breaking of seals or shaking is necessary. And Hexadrol* is so stable it can be stored for up to two years at room temperature.



HEXADROL*

(dexamethasone sodium phosphate injection U.S.P.)

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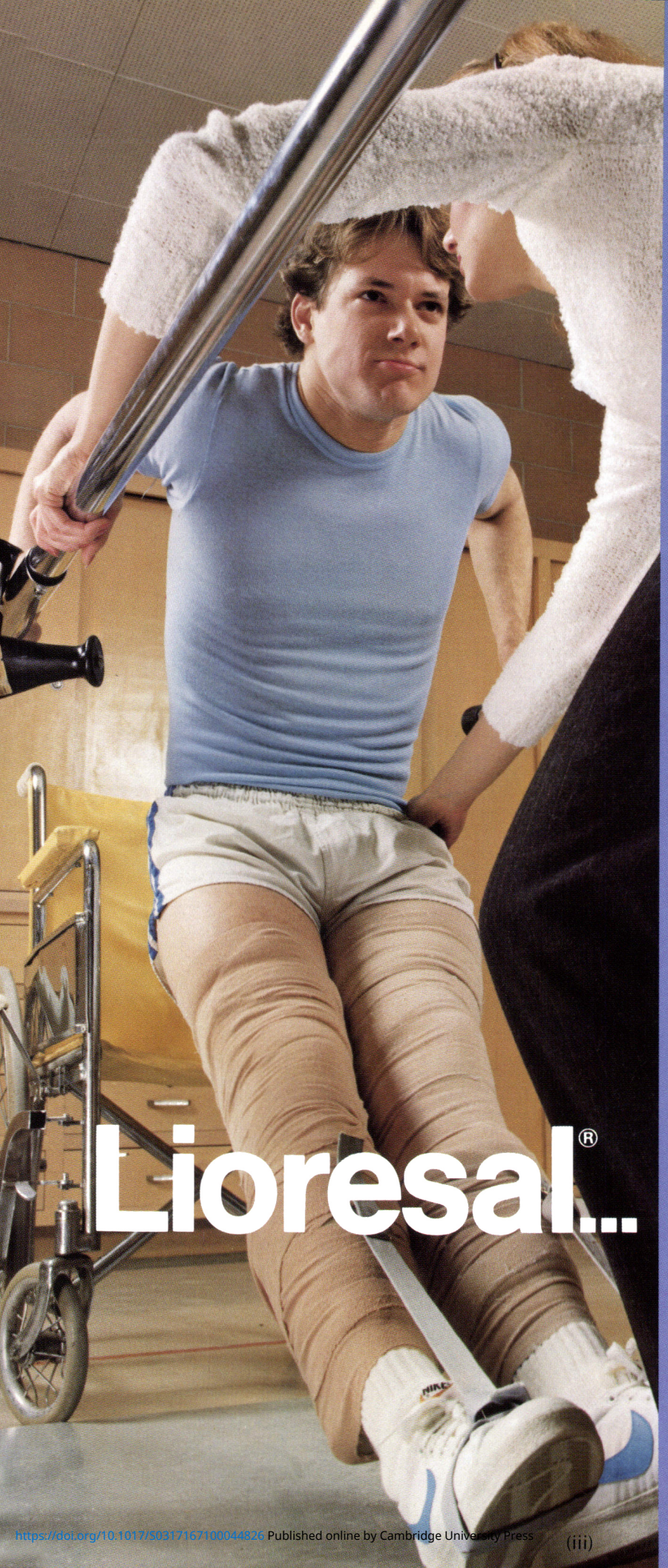

Lioresal®...

Lioresal®
baclofen

Traitez la spasticité **dès le début** pour accélérer son rétablissement.

Une prompte intervention avec le Lioresal, avant qu'une incapacité majeure ne s'installe, peut grandement contribuer à la réadaptation.[1]

- Lioresal aide à soulager la spasticité due aux lésions de la moelle épinière, à la sclérose en plaques et autres affections médullaires.
- Lioresal agit principalement au niveau de la moelle épinière éliminant le risque de sédation excessive gênante.[2]
- Lioresal améliore la perspective d'un traitement prolongé.[1]

avant qu'il ne soit **trop tard.**

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