

DATA SHEET

DEXAMPHETAMINE SULPHATE TABLETS 5mg

Dexamphetamine Sulphate BP

PRESENTATION

White 8mm normal convex tablets each containing 5mg dexamphetamine sulphate.

USES

Actions Dexamphetamine, the dextrorotatory isomer of amphetamine, is an indirect-acting sympathomimetic amine with central stimulant and anorectic activity. It increases motor activity and mental alertness, and diminishes drowsiness and a sense of fatigue.

In children with attention-deficit hyperactivity disorder, dexamphetamine decreases motor restlessness and enhances the ability to pay attention.

Amphetamine facilitates the action of dopamine and norepinephrine by blocking re-uptake from the synapse, inhibits the action of monoamine oxidase (MAO), and facilitates the release of catecholamines. It may also stimulate inhibitory autoreceptors in the *substantia nigra* and *ventral tegmentum*.

Pharmacokinetics Dexamphetamine sulphate is readily absorbed from the gastro-intestinal tract and rapidly distributed into most of the body tissues with high concentrations in the brain and CSF.

The biotransformation is hepatic and the biological half-life is 10 to 12 hours in adults and 6 to 8 hours in children. The main metabolic reaction is oxidative deamination to form phenylacetone, which is then oxidised to benzoic acid and conjugated with glycine to form hippuric acid.

The elimination is mainly renal. Urinary elimination is pH dependent and enhanced in acid urine. A considerable fraction may be excreted in the urine unchanged. Under uncontrolled urinary pH conditions, about 30% of the dose is excreted unchanged in the urine in 24 hours and a total of about 90% of the dose is excreted in 3 to 4 days.

Indications Dexamphetamine sulphate 5mg Tablets are indicated in the treatment of well-established and proven narcolepsy. It is also indicated for children with refractory hyperkinetic states under the supervision of a physician specialising in child psychiatry.

DOSAGE AND ADMINISTRATION

For narcolepsy :

Adults :

Oral, 5 to 20 mg a day in divided doses as needed and tolerated. The usual starting dose is 5mg a day, given in divided doses. Doses may be increased if necessary by 5mg a day at weekly intervals to a suggested maximum of 20mg a day.

Elderly :

Start with 5mg a day, and increase by increments of 5 mg at weekly intervals to a suggested maximum of 20mg a day.

Children :

- Children up to 6 years of age
- Children 6 to 12 years of age

Dosage has not been established.

Oral, 5mg a day, the dosage being increased by 5 mg a day at one-week intervals until the desired response is obtained or until the adult dose is reached.

For attention-deficit hyperactivity disorders :

Children :

- Children up to 3 years of age
- Children 3 to 5 years of age

- Children 6 years of age and over

Use is not recommended.

Oral, 2.5mg once a day, the dosage being increased by 2.5mg a day at one-week intervals until the desired response is obtained.

Oral, 5mg one or two times a day, the dosage being increased by 5mg a day at one-week intervals until the desired response is obtained.

CONTRAINDICATIONS

Dexamphetamine sulphate tablets are contraindicated in patients with known hypersensitivity to dexamphetamine or other amphetamine derivatives or any of the excipients. Do not use in patients with symptomatic cardiovascular disease, structural cardiac abnormalities and/or moderate or severe hypertensive disease.

Do not use in patients with advanced arteriosclerosis.

Do not use in patients during or for 14 days after treatment with MAO inhibitor.

Do not use in patients with a history of drug abuse or alcohol abuse.

Do not use in patients with hyperthyroidism, glaucoma, porphyria or hyperexcitability.

Do not use in patients with Gilles de la Tourette syndrome or similar dystonias.

Dexamphetamine tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

It should be avoided in pregnant women or breast feeding mothers.

WARNINGS AND PRECAUTIONS

Use with caution in patients on guanethidine and patients with mild hypertension or a family history of dystonias. If tics develop, discontinue treatment with dexamphetamine.

Dexamphetamine is likely to reduce the convulsant threshold therefore caution is advised in patients with epilepsy. Height and weight should be carefully monitored in children as growth retardation may occur. Children who are not gaining weight as expected should have their treatment interrupted temporarily.

Caution should be used when administering dexamphetamine to patients with impaired kidney function or unstable personality.

Drug dependence, with consumption of increasing doses to levels many times those recommended, may occur as tolerance develops. At such levels, a psychosis which may be clinically indistinguishable from schizophrenia can occur.

Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression.

Cardiomyopathy has been reported with chronic amphetamine use.

Due to the potential decreased appetite associated with dexamphetamine use, caution is advised in the presence of anorexia nervosa.

Pre-existing structural cardiac abnormalities: Sudden death has been reported in association with the use of stimulants of the central nervous system at usual doses in children with structural cardiac abnormalities. Although some structural cardiac abnormalities alone may carry an increased risk of sudden death, stimulant products are not recommended in children, adolescents, or adults with known structural cardiac abnormalities (see *Contraindications*).

Blood pressure should be monitored at appropriate intervals in all patients taking dexamphetamine, especially those with hypertension.

Psychiatric adverse events:

- Administration of stimulants may exacerbate symptoms of behaviour disturbance and thought disorders in patients with a pre-existing psychotic disorder.
- Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.
- Treatment emergent psychotic or manic symptoms, e.g. hallucinations, delusional thinking or mania in children or adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant and discontinuation of treatment may be appropriate.
- Patients beginning treatment with stimulants for ADHD should be monitored for the appearance, or worsening of, aggressive behaviour or hostility.

Use with caution in patients sensitive to amphetamines and other sympathomimetics.

Pregnancy : Use of dexamphetamine sulphate during pregnancy may be associated with an increased risk of congenital malformations, especially in the cardiovascular system and biliary tract. Reproductive studies in rodents have suggested both an embryotoxic and a teratogenic potential when amphetamines were administered and retrospective evidence of certain significance in man has suggested a similar possibility. Dexamphetamine is contraindicated during pregnancy.

Nursing mothers : Dexamphetamine is passed into breast milk. Because of the potential for adverse reactions in nursing infants from dexamphetamine, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Paediatrics : Prolonged administration of dexamphetamine sulphate to children may inhibit growth. Height and weight in children should be monitored. Psychotic children may experience exacerbation of symptoms of behaviour disturbance and thought disorder. It provokes or exacerbates motor and *vocal tics* and *Tourette's syndrome*, necessitating clinical evaluation before administration of dexamphetamine sulphate.

Geriatrics : No data is available on relationship of age to the effects of dexamphetamine in geriatric patients.

Dexamphetamine may affect ability to drive or operate machinery.

ADVERSE EFFECTS

Cardiac disorders: cardiomyopathy, myocardial infarction, palpitations, tachycardia

Eye disorders: mydriasis, visual disturbance

Gastrointestinal disorders: abdominal cramps, colitis ischaemic, diarrhea, dry mouth, nausea

General disorders and administration site conditions: chest pain, death due to cardiovascular collapse, growth retardation, hyperpyrexia, hypersensitivity including angioedema and anaphylaxis, sudden death.

Investigations: blood pressure decreased, blood pressure increased

Metabolism and nutrition disorders: acidosis, anorexia, weight loss.

Musculoskeletal and connective tissue disorders: rhabdomyolysis

Nervous system disorders: ataxia, choreoathetoid movements, concentration difficulties, convulsion, dizziness, dyskinesia, dysgeusia, fatigue, headache, hyperactivity, hyperreflexia, intracranial haemorrhage, neuroleptic malignant syndrome, stroke, tremor, Tourette's syndrome

Psychiatric disorders: aggressive behaviour, anxiety, confusion, delirium, depression, drug dependence, dysphoria, emotional lability, euphoria, hallucination, impaired cognitive test performance, insomnia, irritability, libido altered, nervousness, night terrors, obsessive-compulsive behavior, panic states, paranoia, psychosis/ psychotic reactions, restlessness, tics

Renal and urinary disorders: renal damage

Reproductive system and breast disorders: impotence

Skin and subcutaneous tissue disorders: alopecia, rash, sweating, urticaria

Vascular disorders: cardiovascular collapse, cerebral vasculitis

A toxic hypermetabolic state, characterised by transient hyperactivity, hyperpyrexia, acidosis and death due to cardiovascular collapse have been reported.

Cessation of, or reduction in, amphetamine use that has been heavy and prolonged can result in withdrawal symptoms. Symptoms include dysphoric mood, fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite, psychomotor retardation or agitation, anhedonia and drug craving.

INTERACTIONS

Adrenoreceptor blocking agents (e.g. propranolol), lithium and α methyltyrosine may antagonise the effects of dexamphetamine. Disulfiram may inhibit metabolism and excretion.

The concurrent use of tricyclic antidepressants may increase the risk of cardiovascular side effects.

Concurrent use of MAOI's or use within the preceding 14 days may precipitate a hypertensive crisis.

Concurrent use of beta-blockers may result in severe hypertension and dexamphetamine may result in diminished effect of other anti-hypertensives such as guanethidine.

Phenothiazines may inhibit the actions of dexamphetamine.

Amphetamines may delay the absorption of ethosuximide, phenobarbital and phenytoin.

Acute dystonia has been noted with concurrent administration of haloperidol.

Haloperidol blocks dopamine and norepinephrine re-uptake, thus inhibiting the central stimulant effects of amphetamines.

The analgesic effect of morphine may be increased and its respiratory depressant effects decreased with concurrent use of morphine and dexamphetamine.

Amphetamines potentiate the analgesic effects of meperidine.

Concomitant administration of clonidine and dexamphetamine may result in an increased duration of action of dexamphetamine.

Gastrointestinal acidifying agents (guanethidine, reserpine, glutamic acid HCl, ascorbic acid, fruit juices, etc.) lower absorption of dexamphetamine. Urinary acidifying agents (ammonium chloride, sodium acid phosphate, etc.) increase urinary excretion of dexamphetamine. Both groups of agents lower blood levels and efficacy of dexamphetamine.

Gastrointestinal alkalizing agents (sodium bicarbonate, etc) increase the absorption of amphetamines. Urinary alkalizing agents (acetazolamide, some thiazides) increase the concentration of the non-ionized species of the amphetamine molecule, thereby decreasing urinary excretion. Both groups of agents increase blood levels and efficacy of amphetamines.

Alcohol may exacerbate the CNS adverse reactions of psychoactive drugs, including dexamphetamine. It is therefore advisable for patients to abstain from alcohol during treatment.

Chlorpromazine blocks dopamine and norepinephrine re-uptake, thus inhibiting the central stimulant effects of amphetamines, and can be used to treat amphetamine poisoning.

OVERDOSAGE

In acute overdosage, the adverse effects are accentuated and may be accompanied by hyperpyrexia, mydriasis, hyperreflexia, chest pain, cardiac arrhythmias, confusion, panic states, aggressive behaviour, hallucinations, delirium, convulsions, respiratory depression, coma, circulatory collapse and death.

Individual patient response may vary widely and toxic manifestations may occur at relatively low doses.

Treatment consists of the induction of vomiting and/or gastric lavage together with supportive and symptomatic measures. Excessive stimulation or convulsions may be treated with diazepam. Excretion of dexamphetamine may be increased by forced acid diuresis. Chlorpromazine antagonizes the central stimulant effects of amphetamines and can be used to treat amphetamine intoxication.

PHARMACEUTICAL PRECAUTIONS

Store below 25⁰C in an air tight container. Protect from light. Do not refrigerate. Shelf life is 24 months from date of manufacture.

MEDICINE CLASSIFICATION

Controlled Drug Class B1.

PACKAGE QUANTITIES

Pack of 100 tablets in amber a glass bottle

FURTHER INFORMATION

This product also contains:

Lactose

Maize Starch

Purified Talc

Magnesium Stearate

Silicon Dioxide

Acacia Gum

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