SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dexamfetamine Sulfate 5 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5mg Dexamfetamine Sulfate

Excipients with known effect:

Each tablet contains 177 mg lactose and 14 mg sucrose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Half scored circular white tablets with bevelled edges marked 'Evans' above and 'DB5' below.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dexamfetamine sulfate is a symphathomimetic amine with central stimulant and anorectic activity. It is indicated in narcolepsy. It is also indicated for children with refractory hyperkinetic states under the supervision of a physician specialising in child psychiatry.

4.2 Posology and method of administration

Posology

Adults: In narcolepsy, the usual starting dose is 10mg dexamfetamine sulfate a day, given in divided doses. Dosage may be increased if necessary by 10mg a day at weekly intervals to a suggested maximum of 60mg a day.

Elderly: Start with 5mg a day, and increase by increments of 5mg at weekly intervals.

Children: In hyperkinetic states, the usual starting dosage for children aged 3-5 years is 2.5mg a day, increased if necessary by 2.5mg a day at weekly intervals; for children aged 6 years and over, the usual starting dose is 5-10mg a day increasing if necessary by 5mg at weekly intervals.

The usual upper limit is 20mg a day though some older children have needed 40mg or more for optimal response.

Method of administration
For oral administration.

4.3 Contraindications

- Hypersensitivity to dexamfetamine or other amfetamine derivatives or any of the excipients listed in section 6.1.
- Patients with symptomatic cardiovascular disease, structural cardiac abnormalities and/or moderate or severe hypertensive disease.
- Patients with advanced arteriosclerosis.
- During or for 14 days after treatment with an MAO inhibitor.
- Patients with a history of drug abuse or alcohol abuse.
- Patients with hyperthyroidism, glaucoma, porphyria or hyperexcitability.
- Patients with Gilles de la Tourette syndrome or similar dystonias.
- Dexamfetamine sulfate tablets include lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Dexamfetamine sulfate tablets include sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- Pregnancy and lactation.

4.4 Special warnings and precautions for use

Use with caution in patients on guanethidine and patients with mild hypertension or a family history of dystonias. If tics develop, discontinue treatment with dexamfetamine sulfate. Dexamfetamine 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 dexamfetamine 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 amfetamine use.

Due to the potential decreased appetite associated with dexamfetamine 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 4.3, Contraindications*).

Blood pressure should be monitored at appropriate intervals in all patients taking dexamfetamine, 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.

4.5 Interaction with other medicinal products and other forms of interaction

Adrenoreceptor blocking agents (e.g. propanolol), lithium and α methyltyrosine may antagonise the effects of dexamfetamine. 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 dexamfetamine may result in diminished effect of other anti-hypertensives such as guanethidine.

Phenothiazines may inhibit the actions of dexamfetamine.

Amfetamines 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 amfetamines.

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

Amfetamines potentiate the analgesic effects of meperidine.

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

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

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

Alcohol may exacerbate the CNS adverse reactions of psychoactive drugs, including dexamfetamine. 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 amfetamines, and can be used to treat amfetamine poisoning.

Drug/laboratory test interactions

Amphetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amphetamines may interfere with urinary steroid determinations.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Dexamfetamine has been thought to produce embroytoxic effects in rodents and retrospective evidence of certain significance in man has suggested a similar possibility.

Dexamfetamine sulfate is contraindicated during pregnancy.

Data from a cohort study of in total approximately 5570 pregnancies exposed to amphetamine in the first trimester do not suggest an increased risk of congenital malformation. Data from another cohort study in approximately 3100 pregnancies exposed to amphetamine during the first 20 weeks of pregnancy, suggest an increased risk of preeclampsia, and preterm birth.

Children of mothers who are dependent on amfetamine have been shown to be at an increased risk of premature birth and reduced birth weight.

Moreover, these children may develop withdrawal symptoms like dysphoria, including hyperexcitability and pronounced exhaustion.

Breastfeeding:
Dexamfetamine sulfate passes into breast milk.

Because of the potential for adverse reactions in nursing infants from dexamfetamine, a decision should be made whether to discontinued nursing or discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Dexamfetamine sulfate may affect ability to drive or operate machinery.
This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in

regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- *The medicine is likely to affect your ability to drive*
- *Do not drive until you know how the medicine affects you*
- *It is an offence to drive while under the influence of this medicine*
- *However, you would not be committing an offence (called 'statutory defence') if:*
  - o *The medicine has been prescribed to treat a medical or dental problem and*
  - o *You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and*
  - o *It was not affecting your ability to drive safely"*

4.8 Undesirable effects

The frequencies of adverse events are ranked according to the following: : very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000) very rare (< 1/10,000) and not known (cannot be estimated from the available data).

Metabolism and nutrition disorders:

Not known: acidosis, anorexia, weight loss

Psychiatric disorders:

Not known: 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

Nervous system disorders:

Not known: ataxia, choreoathetoid movements, concentration difficulties, convulsion, dizziness, dyskinesia, dysgeusia, fatigue, headache, hyperactivity, hyperreflexia, intracranial haemorrhage, neuroleptic malignant syndrome, stroke, tremor

Eye disorders:

Not known: mydriasis, visual disturbance

Cardiac disorders:

Not known: cardiomyopathy, myocardial infarction, palpitations, tachycardia

Vascular disorders:

Not known: cardiovascular collapse, cerebral vasculitis, Raynaud's phenomenon

Gastrointestinal disorders:

Not known: abdominal cramps, colitis ischaemic, diarrhoea, dry mouth, nausea

Skin and subcutaneous tissue disorders:

Not known: alopecia, rash, sweating, urticaria

Musculoskeletal and connective tissue disorders:

Not known: rhabdomyolysis, growth retardation

Renal and urinary disorders:

Not known: renal impairment

Reproductive system and breast disorders:

Not known: impotence

Congenital, familial and genetic disorders:

Not known: Tourette's disorder

General disorders and administration site conditions:

Not known: chest pain, death due to cardiovascular collapse, hyperpyrexia, hypersensitivity including angioedema and anaphylaxis, sudden death *(see 4.4, Special warnings and precautions for use).*

Investigations:

Not known: blood pressure decreased, blood pressure increasedA toxic hypermetabolic state, characterised by transient hyperactivity, hyperpyrexia, acidosis and death due to cardiovascular collapse have been reported.

Cessation of, or reduction in, amfetamine 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme (Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store).

4.9 Overdose

Symptoms

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

Toxicity

Individual patient response may vary widely and toxic manifestations may occur with quite small overdoses.

Treatment

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 dexamfetamine may be increased by forced acid diuresis. Chlorpromazine antagonises the central stimulant effects of amfetamines and can be used to treat amfetamine intoxication.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dexamfetamine sulfate is a sympathomimetic amine with a central stimulant and anorectic activity.

5.2 Pharmacokinetic properties

Absorption
Dexamfetamine is readily absorbed from the gastrointestinal tract. It is resistant to metabolism by monoamine oxidase.

Elimination

Elimination is increased in acidic urine. After high doses, elimination in the urine may take several days. It is excreted in the urine as unchanged parent drug together with some hydroxylated metabolites.

5.3 Preclinical safety data

Dexamfetamine has been thought to produce embryotoxic effects in rodents, and retrospective evidence of uncertain significance in man has suggested a similar possibility. Dexamfetamine sulfate passes into breast milk.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stearic acid

Acacia powder

Lactose

Paraffin, Light Liquid

Maize starch

Sucrose

Purified talc

Purified water

6.2 Incompatibilities

None stated

6.3 Shelf life

5 years

6.4 Special precautions for storage

No special storage precautions are necessary.

6.5 Nature and contents of container

Polypropylene securitainers, amber glass bottles or polythene vials containing 1000 and 100 tablets. Blister packs containing 100 and 28 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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