SUMMARY OF PRODUCT CHARACTERISTICS

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1 NAME OF THE MEDICINAL PRODUCT

Dexamfetamine Sulfate 1 mg/ ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 1 mg dexamfetamine sulfate.

Excipient with known effect:

1 ml oral solution contains 200 mg liquid maltitol and 0.6 mg benzoic acid.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

The oral solution is clear and colourless.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Narcolepsy

Dexamfetamine sulfate is indicated in the treatment of narcolepsy in adults.

ADHD

Dexamfetamine is also indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children and adolescents aged 6 to 17 years when response to previous methylphenidate treatment is considered clinically inadequate. A comprehensive treatment programme typically includes psychological, educational and social measures.

Diagnosis should be made according to DSM-5 criteria or the guidelines in ICD-10 and should be based on a comprehensive multidisciplinary evaluation of the patient.

Dexamfetamine is not indicated in all children with ADHD and the decision to use dexamfetamine must be based on a very thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age and potential for abuse, misuse or diversion.

Treatment should be under the supervision of a specialist in childhood and/or adolescent behavioural disorders.

4.2 Posology and method of administration

Narcolepsy

Adults:

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

Elderly:

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

ADHD

Treatment must be under the supervision of a specialist in childhood and/or adolescent behaviour disorders.

Careful dose titration is necessary at the start of treatment with dexamfetamine. Dose titration should be started at the lowest possible dose.

The recommended starting daily dose is 5 mg once or twice daily (e.g. at breakfast and lunch), increasing if necessary by weekly increments of 5mg in the daily dose according to tolerability and degree of efficacy observed.

In the treatment of ADHD, the times at which the doses of Dexamfetamine Sulfate 1 mg/ ml Oral Solution are administered should be selected to provide the best effect when it is most needed to combat school and social behavioural difficulties. Normally the first increasing dose is given in the morning. Dexamfetamine Sulfate 1 mg/ ml Oral Solution should not be taken too late after lunch time to avoid disturbances of sleep.

The regimen that achieves satisfactory symptom control with the lowest total daily dose should be employed.

The maximum daily dose in children and adolescents usually is 20 mg, although doses of 40 mg may in rare cases be necessary for optimum titration.

Long-term use

Long-term usefulness of dexamfetamine for extended periods (over 12 months) in children and adolescents with ADHD should be periodically re-evaluated for the individual patient with trial periods off medication to assess the patient's functioning without pharmacotherapy. It is recommended that dexamfetamine is de-challenged at least once yearly to assess the child's condition (preferably during times of school holidays). Improvement may be sustained when the medicinal product is either temporarily or permanently discontinued.

Dose reduction and discontinuation

Treatment must be stopped if the symptoms do not improve after appropriate dosage adjustment over a one-month period. If paradoxical aggravation of symptoms or other serious adverse events occur, the dosage should be reduced or discontinued.

Special populations

Children under 6 years of age

The safety and efficacy of Dexamfetamine Sulfate 1 mg/ ml Oral Solution in children aged 0 to 6 years has not been established.

Therefore Dexamfetamine Sulfate 1 mg/ ml Oral Solution should not be used in children under the age of 6 years.

Adults

Dexamfetamine sulfate is not licensed for use in adults. The safety and efficacy of dexamfetamine in adults have not been established.

Elderly

Dexamfetamine Sulfate 1 mg/ ml Oral Solution should not be used in the elderly. Safety and efficacy of dexamfetamine has not been established in this age group.

Patients with renal or hepatic insufficiency

There is no experience with the use of dexamfetamine in patients with renal or hepatic insufficiency.

Thus, dexamfetamine should be used with special caution in this patient group by taking care of titration and dosage

Method of administration:

For oral administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

- Known hypersensitivity to sympathomimetic amines
- Glaucoma
- Phaeochromocytoma
- Symptomatic cardiovascular disease, structural cardiac abnormalities and/or moderate or severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias and channelopathies (disorders caused by the dysfunction of ion channels)
- Advanced arteriosclerosis
- Concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days of MAOI treatment
- Hyperthyroidism or thyrotoxicosis.
- Severe depression, anorexia nervosa/anorexic disorders, suicidal ideation, hyperexcitability, psychotic symptoms, severe and episodic (Type I) Bipolar (affective) Disorder (that is not well-controlled), schizophrenia, psychopathic/borderline personality disorder

- Gilles de la Tourette syndrome or similar dystonias.
- Cerebrovascular disorders (cerebral aneurysm, vascular abnormalities including vasculitis or stroke)
- Porphyria
- History of drug abuse or alcohol abuse

4.4 Special warnings and precautions for use

Precautions to be taken before handling or administering the medicinal product

Pre-treatment screening:

Prior to prescribing, it is necessary to conduct a baseline evaluation of a patient's cardiovascular status including blood pressure and heart rate. A comprehensive history should document concomitant medications, past and present co-morbid medical and psychiatric disorders or symptoms, family history of sudden cardiac/unexplained death and accurate recording of pre-treatment height and weight on a growth chart (see sections 4.3 and 4.4)

Ongoing monitoring

Growth, psychiatric and cardiovascular status should be continuously monitored (see also Section 4.4).

- Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months;

- Height, weight and appetite should be recorded at least 6 monthly with maintenance of a growth chart;

- Development of de novo or worsening of pre-existing psychiatric disorders, including depression and aggressive behaviour, should be monitored at every adjustment of dose and then at least every 6 months and at every visit.

Patients should be monitored for the risk of diversion, misuse, and abuse of

dexamfetamine Long-term use (more than 12 months) in children and

adolescents

The safety and efficacy of long-term use of dexamfetamine has not been systematically evaluated in controlled trials. Dexamfetamine treatment should not be and does not need to be indefinite.
Dexamfetamine treatment is usually discontinued during or after puberty. Patients on long-term therapy (i.e. over 12 months) must have careful ongoing monitoring according to the guidance in sections 4.2 and 4.4 for cardiovascular status, growth,

appetite, and development of de novo or worsening of pre-existing psychiatric disorders. Psychiatric disorders to monitor for are described below, and include (but are not limited to) motor or vocal tics, aggressive or hostile behaviour, agitation, anxiety, depression, psychosis, mania, delusions, irritability, lack of spontaneity, withdrawal, and excessive perseveration.

The physician who elects to use dexamfetamine for extended periods (over 12 months) in children and adolescents with ADHD should periodically re-evaluate the long-term usefulness of the medicinal product for the individual patient with trial periods off medication to assess the patient's functioning without pharmacotherapy. It is recommended that dexamfetamine is de-challenged at least once yearly to assess the child's condition (preferably during times of school holidays). Improvement may be sustained when the medicinal product is either temporarily or permanently discontinued.

Cardiovascular status

Patients who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden cardiac or unexplained death or malignant arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further specialist cardiac evaluation if initial findings suggest such history or disease. Patients who develop symptoms such as palpitations, exceptional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of cardiac disease during dexamfetamine treatment should undergo a prompt specialist cardiac evaluation.

Cardiovascular status should be carefully monitored. Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months.

Treatment with stimulants in general may lead to a minor increase in blood pressure (approx. 2-4 mm Hg) as well as an increase in heart rate (approx. 3-6 beats/minute). In few patients, these values may be higher.

The short- and long-term clinical consequences of these cardiovascular effects in children and adolescents are not known, but the possibility of clinical complications cannot be excluded as a result of the effects observed in the clinical trial data. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate. See section 4.3 for conditions in which dexamfetamine treatment in contraindicated.

The use of dexamfetamine is contraindicated in certain pre-existing cardiovascular disorders unless specialist cardiac advice has been obtained (see section 4.3).

Sudden death and pre-existing cardiac structural abnormalities or other serious cardiac disorders

Sudden death has been reported in association with the use of stimulants of the central nervous system at usual doses in children, some of whom had cardiac structural abnormalities or other serious heart problems. Although some serious heart problems alone may carry an increased risk of sudden death, stimulant products are not recommended in patients with known cardiac structural abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the onset of sympathomimetic effects of a stimulant medicine (see section 4.3).

Cardiovascular events

Misuse of stimulants of the central nervous system may be associated with sudden death and other serious cardiovascular adverse events.

Cases of cardiomyopathy have been observed with chronic use of

amfetamine. Cerebrovascular disorders

See section 4.3 for cerebrovascular conditions in which dexamfetamine treatment is contraindicated. Patients with additional risk factors (such as a history of cardiovascular disease or concomitant medications that elevate blood pressure) should be assessed at every visit for neurological signs and symptoms after initiating treatment with dexamfetamine.

Cerebral vasculitis appears to be a very rare idiosyncratic reaction to dexamfetamine exposure. There is little evidence to suggest that patients at higher risk can be identified and the initial onset of symptoms may be the first indication of an underlying clinical problem. Early diagnosis, based on a high index of suspicion, may allow the prompt withdrawal of dexamfetamine and early treatment. The diagnosis should therefore be considered in any patient who develops new neurological symptoms that are consistent with cerebral ischemia during dexamfetamine therapy. These symptoms could include severe headache, numbness, weakness, paralysis, and impairment of coordination, vision, speech, language, or memory.

Treatment with dexamfetamine is not contraindicated in patients with hemiplegic cerebral

palsy. Psychiatric disorders

Comorbidity of psychiatric disorders in ADHD is common and should be taken into account when prescribing stimulant products. In the case of emergent psychiatric symptoms or exacerbation of pre- existing psychiatric disorders, dexamfetamine should not be given unless the benefits outweigh the risks to the patient.

Development or worsening of psychiatric disorders should be monitored at every adjustment of dose, then at least every 6 months, and at every visit; discontinuation of treatment may be appropriate.

Exacerbation of pre-existing psychotic or manic symptoms

In psychotic patients, administration of dexamfetamine may exacerbate symptoms of behavioural disturbance and thought disorder.

Emergence of new psychotic or manic symptoms

Treatment-emergent psychotic symptoms (visual/tactile/auditory hallucinations and delusions) or mania in children and adolescents without prior history of psychotic illness or mania can be caused by dexamfetamine at usual doses.

A pooled analysis of various short-term, placebo-controlled studies revealed that such symptoms

occurred in approx. 0.1% of patients (4 out of 3,482) who were treated with dexamfetamine or amfetamine for several weeks, whereas none of the patients of the placebo group were affected by these symptoms.

If manic or psychotic symptoms occur, consideration should be given to a possible causal

role for dexamfetamine, and discontinuation of treatment may be appropriate.

Aggressive or hostile behaviour

The emergence or worsening of aggression or hostility can be caused by treatment with stimulants. Patients treated with dexamfetamine should be closely monitored for the emergence or worsening of aggressive behaviour or hostility at treatment initiation, at every dose adjustment and then at least every 6 months and at every visit. Physicians should evaluate the need for adjustment of the treatment regimen in patients experiencing behaviour changes.

Suicidal ideation

Patients with emergent suicidal ideation or behaviour during treatment should be evaluated immediately by their physician. Consideration should be given to the exacerbation of an underlying psychiatric condition and to a possible causal role of dexamfetamine treatment. Treatment of an underlying psychiatric condition may be necessary and consideration should be given to a possible discontinuation of dexamfetamine.

Tics

Dexamfetamine is associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported. Family history should be assessed and clinical evaluation for tics or Tourette's syndrome in children should precede the use of dexamfetamine. Patients should be regularly monitored for the emergence or worsening of tics during treatment with dexamfetamine. Monitoring should be at every adjustment of dose and then at least every 6 months or every visit.

Anxiety, agitation, or tension

Dexamfetamine is associated with the worsening of pre-existing anxiety, agitation, or tension. Clinical evaluation for anxiety, agitation or tension should precede use of dexamfetamine and patients should be regularly monitored for the emergence or worsening of these symptoms during treatment, at every adjustment of dose and then at least every 6 month or at every visit.

Forms of bipolar disorder

Particular care should be taken in using dexamfetamine to treat patients with comorbid bipolar disorder (including untreated type I bipolar disorder or other forms of bipolar disorder) because of concerns for possible precipitation of a mixed/manic episode in such patients. Prior to initiating treatment with dexamfetamine, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder. Such a screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. Close ongoing monitoring is essential in these patients (see above 'Psychiatric disorders' and section 4.2). Patients should be monitored for symptoms at every adjustment of dose, then at least every 6 months and at every visit.

Growth

Moderately reduced weight gain and growth retardation have been reported with the long-term use of dexamfetamine in children.

The effects of dexamfetamine on final height and final weight are currently unknown and being studied.
Growth should be monitored during dexamfetamine treatment: height, weight and appetite should be

recorded at least 6 monthly with maintenance of a growth chart. Patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.
As a reduction in appetite may occur during treatment with dexamfetamine, the medicinal product may only be administered with special caution to patients with Anorexia nervosa.

Seizures

Dexamfetamine should be used with caution in patients with epilepsy. Dexamfetamine may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in the absence of seizures, and rarely in patients without a history of convulsions and no EEG abnormalities. If seizure frequency increases or new-onset seizures occur, dexamfetamine should be discontinued.

Abuse, misuse, and diversion

Patients should be carefully monitored for the risk of diversion, misuse, and abuse of dexamfetamine.

The risk is generally greater for short acting stimulants than for corresponding long-acting products (see section 4.1).

Dexamfetamine should not be used in patients with known drug or alcohol dependency because of a potential for abuse, misuse, or diversion.

Chronic abuse of dexamfetamine can lead to marked tolerance and psychological dependence with varying degrees of abnormal behaviour. Frank psychotic episodes can occur, especially in response to parenteral abuse.

Signs of chronic amfetamine intoxication include severe dermatoses, pronounced sleeplessness, confusion, hyperactivity, and personality changes. The most severe sign of chronic amfetamine intoxication is a psychosis which in most cases can hardly be clinically distinguished from schizophrenia. However, such a psychosis rarely occurs after oral ingestion of amfetamines. There have also been reports of intracerebral bleeding. Serious cardiovascular events observed in association with amfetamine misuse were sudden death, cardiomyopathy, and myocardial infarction.

Patient age, the presence of risk factors for substance use disorder (such as comorbid oppositional- defiant or conduct disorder and bipolar disorder), previous or current substance abuse should all be taken into account when deciding on a course of treatment. Caution is called for in emotionally unstable patients, such as those with a history of drug or alcohol dependence, because such patients may increase the dosage on their own initiative.

For some high-risk substance abuse patients, dexamfetamine or other stimulants may not be suitable. This may also be true for other stimulants and therefore, non-stimulant treatment should be considered.

Withdrawal

Careful supervision is required during withdrawal of the medicinal product, since this may unmask depression as well as chronic over-activity. Some patients may require long-term follow up.

Similarly, careful supervision is required during withdrawal from abusive use since severe depression may occur.

Abrupt withdrawal after a prolonged period of intake of high doses of dexamfetamine may cause extreme fatigue as well as changes in the EEG during sleep.

Fatigue

Dexamfetamine should not be used for the prevention or treatment of normal fatigue states.

Drug screening

This product contains dexamfetamine which may induce a positive laboratory test for amfetamines, particularly with an immunoassay screening test.

Renal or hepatic insufficiency

There is no experience with the use of dexamfetamine in patients with renal or hepatic insufficiency. In those patients peak plasma levels could be higher and elimination could be prolonged. Thus, dexamfetamine should be used with special caution in this patient group by taking care of titration and dosage.

Haematological effects

The long-term safety of treatment with dexamfetamine is not fully known. In the event of leukopenia, thrombocytopenia, anaemia, or other alterations, including those indicative of serious renal or hepatic disorders, discontinuation of treatment should be considered.

This medicinal product contains liquid maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

This medicinal product contains 0.6 mg benzoic acid in each ml. Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

4.5 Interaction with other medicinal products and other forms of interaction

Because of possible hypertensive crisis, dexamfetamine is contraindicated in patients being treated (currently or within the preceding 2 weeks) with non-selective, irreversible MAO-inhibitors (see section 4.3).

It is not known whether dexamfetamine may inhibit or induce cytochrome P450 (CYP) enzymes. Co- administration of CYP substrates with narrow therapeutic index should therefore be made with caution.

Dexamfetamine is in part metabolised via CYP2D6. Although the clinical significance of this interaction is likely to be minimal, attention should be paid when medications metabolised by these pathways are administered.

It is not known to which degree dexamfetamine metabolism is dependent on other CYP enzymes. Co- administration of potent inhibitors or inducers of CYP enzymes

should be made with caution.

Agents that lower blood levels of amphetamines

Gastrointestinal acidifying agents (guanethidine, reserpine, glutamic acid HCl, ascorbic acid, fruit juices, etc.) lower the absorption of amfetamines.

Agents that increase blood levels of amphetamines

Urinary acidifying agents (ammonium chloride, sodium acid phosphate, etc.) increase the concentration of the ionized species of the amfetamine molecule, thereby increasing urinary excretion. Both groups of agents lower blood levels and efficacy of amfetamines.

Gastrointestinal alkalinizing agents (sodium bicarbonate, etc.) increase the absorption of amfetamines. Urinary alkalinizing 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 therefore potentiate the actions of amfetamines.

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

Agents whose effects may be reduced by amfetamines

Dexamfetamine may counteract the sedative effect of antihistamines.

Dexamfetamine may inhibit the antihypertensive action of guanethidine or clonidine. Concomitant use of beta-blockers may lead to severe hypertonia, as the therapeutic action of these agents may be inhibited by dexamfetamine.

Depressant effects of opiates, e.g. respiratory depression, may be decreased by dexamfetamine.

Agents whose effects may be increased by amphetamines

Halogenated narcotics**:** There is a risk of sudden blood pressure increase during surgery. If surgery is planned, dexamfetamine treatment should not be used on the day of surgery.

Concomitant use of tricyclic antidepressants may increase the risk of cardiovascular adverse events. Because of a possible increase in blood pressure, special caution is advised if Dexamfetamine Sulfate 1 mg/ ml Oral Solution is administered to patients being treated with vasopressors (see also sections on cardiovascular and cerebrovascular conditions in section 4.4).

Dexamfetamine may enhance the adrenergic effect of

noradrenaline. Dexamfetamine may potentiate the analgesic

effects of meperidine.

The analgesic action of morphine may be potentiated by the concomitant use of dexamfetamine,

Amphetamines can cause a significant elevation in plasma corticosteroid levels. This

increase is greatest in the evening. Amphetamines may interfere with urinary steroid determinations.

Agents that may increase the effects of amphetamines

There are reports indicating that dexamfetamine may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (e.g. phenobarbital, phenytoin, and primidone) and some antidepressants (tricyclics and selective serotonin reuptake inhibitors). When starting or stopping treatment with dexamfetamine, it may be necessary to adjust the dosage of these medicinal products already being taken and establish drug plasma concentrations (or for coumarin, coagulation times).

Disulfiram may inhibit the metabolism and excretion of dexamfetamine.

Agents that may reduce the effects of amphetamines

Adrenergic blockers (e.g. propranolol), lithium, and α-methyltyrosine may attenuate the effects of dexamfetamine.

Concomitant use of haloperidol may inhibit the central stimulant effects of dexamfetamine. Acute dystonia has been noted with concurrent administration of haloperidol.

The absorption of anticonvulsants (e.g. phenobarbital, phenytoin, primidone, and ethosuximide) may be delayed by dexamfetamine.

Use with alcohol

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

Phenothiazines, e.g. chlorpromazine block dopamine receptors, thus inhibiting the central stimulant effects of amfetamines, and can be used to treat amfetamine poisoning.

4.6 Fertility, Pregnancy and lactation

Pregnancy

There is a limited amount of data from the use of dexamfetamine in pregnant women.

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.

Results of studies in animals suggest that high doses of dexamfetamine may elicit reproductive toxicity (see section 5.3).

The use of dexamfetamine during pregnancy is not recommended. Women of childbearing age should discontinue the use of dexamfetamine when intending to become pregnant.

Breast-feeding

Dexamfetamine is excreted in human milk. A risk to the newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from dexamfetamine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Dexamfetamine can cause dizziness, drowsiness and visual disturbances including difficulties with accommodation, diplopia and blurred vision. It may have a moderate influence on the ability to drive and use machines. Patients should be warned of these possible effects and advised that if affected, they should avoid potentially hazardous activities such as driving or operating machinery.

4.8 Undesirable effects

Information on the frequency of these effects was obtained from published clinical studies and meta-analyses as well as the MHRA safety information.

Side-effect assessment is based on the following categories**:**

very common (≥ 1/10)

common (≥ 1/100 to < 1/10)

uncommon (≥ 1/1,000 to <1/100)

rare (≥ 1/10,000 to <1/1,000)

very rare (<1/10,000)

not known (cannot be estimated from the available data).

Blood and lymphatic system disorders

Very rare: Anaemia, leukopenia, thrombocytopenia, thrombocytopenic purpura

Cardiac disorders

Common: Arrhythmia, palpitations, tachycardia

Rare: Angina pectoris

Very rare: Cardiac arrest

Not known: Cardiomyopathy, myocardial infarction

Congenital, familial and genetic disorders

Very rare: Tourette's syndrome

Eye disorders

Rare: Difficulties in visual accommodation, blurred vision, mydriasis

Gastrointestinal disorders

Common: Abdominal pain and cramps, nausea, vomiting, dry mouth

These effects usually occur at the beginning of treatment and may be alleviated by concomitant food intake.

Not known: Ischaemic colitis, diarrhoea

-

General disorders and administration site conditions

- Not known: Chest pain, hyperpyrexia, fatigue, sudden death (see section 4.4)
-

Hepatobiliary disorders

Very rare: Abnormal liver function ranging from hepatic enzyme elevations to hepatic coma

Immune system disorders

- Not known hypersensitivity including angioedema and anaphylaxis
-

Investigations

Common: Changes in blood pressure and heart rate (usually increases)

Metabolism and nutrition disorders

Very common: Decreased appetite, reduced weight gain and weight loss during prolonged use in children

Not known: Acidosis

Musculoskeletal and connective tissue disorders

Common: Arthralgia

Rare: growth retardation during prolonged use in children

Very rare: Muscle cramps

Not known: Rhabdomyolysis

Nervous system disorders

Common: Vertigo, dyskinesia, headache, hyperactivity

Rare: Fatigue

Very rare: Convulsions, choreoathetoid movements, intracranial haemorrhage

Not known: Ataxia, dizziness, dysgeusia, concentration difficulties, hyperreflexia, stroke, tremor

Very rarely, cases of neuroleptic malignant syndrome (NMS) were observed. However, these reports were poorly documented and in most cases, patients were also receiving other medicinal products. Thus, the role of dexamfetamine in the development of NMS is unclear.

Psychiatric disorders

Very common: Insomnia, nervousness

Common: Abnormal behaviour, aggression, excitation, anorexia, anxiety, depression, irritability

Very rare: Hallucinations, psychosis / psychotic reactions, suicidal behaviour (including completed suicide), tics, worsening of pre-existing tics

Not known: Confusion, dependence, dysphoria, emotional lability, euphoria, impaired cognitive test performance, altered libido, night terrors, obsessive-compulsive behaviour, panic states, paranoia, restlessness

Renal and urinary disorders

Not known: Renal damage

Reproductive system and breast disorders

Not known: Impotence

Skin and subcutaneous tissue disorders

Rare: Rash, urticaria

Very rare: Erythema multiforme, exfoliative dermatitis, fixed drug eruption

Not known: Sweating, alopecia

Vascular disorders

Very rare: Cerebral vasculitis and/or occlusion

Not known: Cardiovascular collapse, Raynaud's phenomenon

A 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 at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Signs and symptoms

Acute overdose, mainly due to overstimulation of the central and sympathetic nervous systems, may result in vomiting, agitation, aggression, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, mydriasis, dryness of mucous membranes, flushing, headache, hyperpyrexia, chest pain, tachycardia, palpitations, cardiac arrhythmias, hypertension, respiratory depression, coma, circulatory collapse, and death.

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

Treatment

There is no specific antidote to dexamfetamine overdose. Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. If the signs and symptoms are not too severe and the patient is conscious, gastric contents may be evacuated by induction of vomiting when the medicinal product has been taken less than one hour before. Other measures to detoxify the gut include administration of activated charcoal and a cathartic.

Excessive stimulation or convulsions may be treated with benzodiazepines.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychoanaleptics; psychostimulants, agents used for ADHD and nootropics; centrally acting sympathomimetics, ATC code: N06BA02.

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

5.2 Pharmacokinetic properties

Dexamfetamine is readily absorbed from the gastrointestinal tract. Dexamfetamine is in part metabolised via CYP2D6. It is resistant to metabolism by monoamine oxidase. It is excreted in the urine as unchanged parent drug together with some hydroxylated metabolites. Elimination is increased in acidic urine. After high doses, elimination in the urine may take several days.

5.3 Preclinical safety data

Animal studies on general toxicity, safety pharmacology, genotoxicity and carcinogenicity of dexamfetamine did not reveal any adverse effects not already known in humans.

In studies on the reproductive toxicity of dexamfetamine in mice an increased risk of malformations was observed at dose levels substantially higher than human dose levels. In rats and rabbits, no embryotoxic effects were observed at dose levels above human dose levels.

Behavioural studies in rodents revealed developmental delay, behavioural sensitization as well as increased motor activity in offspring after prenatal exposures to dexamfetamine at dose levels comparable to human therapeutic dose levels. The clinical relevance of these findings is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzoic acid (E210)

Citric acid monohydrate (E330)

Disodium phosphate dihydrate

Liquid maltitol (E965)

Hypromellose

Orange tangerine flavour

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years

Use within 30 days of first opening

6.4 Special precautions for storage

Store the bottle in an upright position

6.5 Nature and contents of container

Amber glass bottles (Type III) with child-proof and tamper-evident white caps (HDPE/PP/LDPE).

Pack size: 150 ml.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Rosemont Pharmaceuticals Ltd
Rosemont House
Yorkdale Industrial Park
Braithwaite Street
Leeds
LS11 9XE
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00427/0282

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/05/2015

10 DATE OF REVISION OF THE TEXT

31/08/2023