Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Dexatin 5 mg tablet
Dexatin 10 mg tablet
Dexatin 20 mg tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dexatin 5 mg tablet
Each tablet contains 5 mg dexamfetamine sulfate.

Dexatin 10 mg
Each tablet contains 10 mg dexamfetamine sulfate.

Dexatin 20 mg
Each tablet contains 20 mg dexamfetamine sulfate.

Excipient with known effect:
5 mg: Isomalt (E953) 153.5 mg
10 mg: Isomalt (E953) 148.5 mg
20 mg: Isomalt (E953) 138.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Dexatin 5 mg tablet
White, round, cloverleaf-shaped tablets of 8.5 mm diameter with a crossed score line on one side and a crossed score line embossed with ”S” on each quarter on the other side.
The tablets can be divided into four equal parts.

Dexatin 10 mg tablet
White, octagonal tablets of 8.1 mm diameter with a crossed score line on one side and a crossed score line embossed with ”M” on each quarter on the other side.
The tablets can be divided into four equal parts.

Dexatin 20 mg tablet
White, round tablets of 8.5 mm diameter with a crossed score line on the one and a crossed score line embossed with ”L” on each quarter on the other side.
The tablets can be divided into four equal parts.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Dexamfetamine is indicated as part of a comprehensive treatment program 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.

Diagnosis should be made according to current DSM criteria or the guidelines in ICD-10 and should be based on a complete anamnesis and a comprehensive multidisciplinary evaluation of the patient. Diagnosis cannot be made solely on the presence of one or more symptoms.

Treatment should be under the supervision of a physician specialized in child and adolescent psychiatry or child and adolescent medicine. A comprehensive treatment program typically includes psychological, educational, and social measures.

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.

Assessment to an appropriate educational training setup is essential, and psychosocial intervention is generally necessary.

4.2 Posology and method of administration

Treatment should be under the supervision of a physician specialized in child and adolescent psychiatry or child and adolescent medicine.

Precautions to be taken before handling or administering the medicinal product.

Pre-treatment evaluation

Prior to prescribing, it is necessary to conduct a baseline evaluation of the patient's cardiovascular status including blood pressure and heart rate. A comprehensive anamnesis should document concomitant medications, present and past 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 section 4.3 and section 4.4).

Consistent with other stimulants, the potential for abuse, misuse, or diversion of dexamfetamine should be considered prior to prescribing (see section 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 dose adjustment and at least every six months.
- Height, weight, and appetite should be recorded at least six-monthly using a growth chart.
- Development of new or worsening of pre-existing psychiatric disorders, including depression and aggressive behaviour, should be monitored at every dose adjustment and then at least every six months and at every visit.

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

Posology

Dose titration should be started at the lowest possible dose. Careful dose titration is necessary at the start of treatment with dexamfetamine. The dose should be individualized according to therapeutic needs and response of the patient.

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 5 mg in the daily dose according to tolerability and degree of efficacy observed.

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. The decision to give Dexatin once or twice daily should be based on the course of symptoms at different times of the day.

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

In the treatment of hyperkinetic disorders/ADHD, the times at which the doses of Dexatin 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. Dexatin should not be taken too late after lunch time to avoid sleep disturbances.

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 terminated 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.
Upon discontinuation, slowly taper off the medication to avoid or reduce withdrawal symptoms.

Special populations
Children under 6 years of age
Dexatin should not be used in children under the age of 6 years. The safety and efficacy of dexamfetamine in children aged 0 to 6 years has not been established.

Use in adults
Dexatin is not approved for use in adults. Safety and efficacy of dexamfetamine in adults have not been established.

Elderly
Dexatin should not be used in the elderly. Safety and efficacy of dexamfetamine have not been established in this age group.

Patients with renal or hepatic impairment
There is no experience with the use of dexamfetamine in patients with renal or hepatic impairment. 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 careful titration of the dose.

Method of administration
Oral use
The tablets may be swallowed whole with the aid of liquids, or alternatively, in cases of swallowing problems or to obtain four equal doses, the tablets can be divided.

For division, the tablet is placed onto a hard surface with its cross-scored, convex side downwards. Then push carefully with the index finger at the centre of its top side. The tablet then breaks into four parts. The divided tablets should be taken together with fluids, e.g. water.

The effect of food on the absorption of dexamfetamine from Dexatin tablets has not been studied, therefore, a possible effect of food on absorption cannot be excluded. Therefore, it is recommended that Dexatin tablets should be taken in a standardized manner in relation to the timing of meals, i.e. doses should be given

at the same times, relative to the time of meals, on each day, preferably with or immediately after meals.

In case of missed dose, Dexatin dosing can resume the next day as planned. Afternoon doses should be avoided because of the potential for insomnia.

4.3 Contraindications

- Hypersensitivity to the active substance or any of the excipients listed in section 6.1
- Hypersensitivity to sympathomimetic amines
- Glaucoma
- Phaeochromocytoma
- Symptomatic cardiovascular disease, structural cardiac abnormalities and/or moderate or severe hypertension, heart failure, arterial occlusive disease, angina, hemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life- threatening arrhythmias and channelopathies (disorders caused by the dysfunction of ion channels)
- Concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days of MAOI treatment
- Hyperthyroidism or thyrotoxicosis
- Severe depression, anorexia nervosa/anorexic disorders, hyperexcitability, suicidal ideation, psychotic symptoms, severe and episodic (type I) bipolar (affective) disorder (that is not well- controlled), schizophrenia, psychopathic/borderline personality disorder
- Tourette's syndrome or similar dystonias
- Cerebrovascular disorders (cerebral aneurysm, vascular abnormalities including vasculitis or stroke)
- Porphyria
- History of drug- or alcohol abuse.

4.4 Special warnings and precautions for use

Long-term treatment (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, limited in time. Dexamfetamine treatment is usually discontinued during or after puberty. Patients on long-term treatment (more than 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 new 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 (more than 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.

Withdrawal

Careful supervision is required during withdrawal of the medicinal product since this may unmask depression or 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 long-term use of high doses of dexamfetamine may cause extreme fatigue as well as changes in the EEG during sleep.

Prescribing and dispensing

The least amount of dexamfetamine feasible should be prescribed or dispensed in order to minimize the risk of possible overdose.

Abuse, misuse, or diversion

Patients should be carefully monitored for the risk of diversion, misuse, and abuse of dexamfetamine. The risk is generally higher for short acting stimulants than for corresponding long-acting products (see section 4.1).

Particular care should be taken when treating elderly children and adolescents.

Dexamfetamine should not be used in patients with drug- or alcohol dependency due to a potential risk of abuse, misuse, or diversion.

Chronic abuse of dexamfetamine may lead to marked development of tolerance and psychological dependence with varying degrees of abnormal behaviour. Frank psychotic episodes may 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 abuse (such as comorbid oppositional-defiant or conduct disorder and bipolar disorder), previous or current drug abuse should all be taken into account when deciding on a course of treatment for ADHD. Caution is called for in emotionally unstable patients, such as those with a history of drug- or alcohol dependence since such patients may increase the dosage on their own initiative.

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

Suicidal ideation

Patients with emergent suicidal ideation or behaviour during treatment for ADHD 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.

Cardiovascular status

Patients who are being considered for treatment with stimulant medications should have a careful anamnesis (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. Further cardiac evaluation by a specialist should be performed if initial findings suggest such anamnesis or disease. Patients who develop symptoms such as palpitations, effort-induced chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of cardiac disease during dexamfetamine treatment should undergo an immediate cardiac evaluation by a specialist.

Cardiovascular status should be carefully monitored. Blood pressure and pulse should be recorded on a centile chart at each dose adjustment 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 may be compromised by increases in blood pressure or heart rate. See section 4.3 for conditions in which dexamfetamine treatment is contraindicated.

The use of dexamfetamine is contraindicated in certain pre-existing cardiovascular disorders unless advice from a paediatric cardiac specialist 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, stimulants are not recommended in children or adolescents 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 CNS-stimulants may be associated with sudden death and other serious cardiovascular adverse events.

Cases of cardiomyopathy have been observed at chronic use of amfetamine.

Assessment of cardiovascular status in patients treated with stimulants

The anamnesis (including assessment for a family history of sudden death or ventricular arrhythmia) should be carefully reviewed in patients considered for treatment with stimulant medications, and a medical exam should be performed to assess the presence of cardiac disease. Further cardiac evaluation should be performed if findings suggest such disease (e.g. electrocardiogram [EKG] or ultrasound examination). Patients who develop symptoms such as effort-induced chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulants treatment should undergo a immediate cardiac evaluation.

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, 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 immediate 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 may 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 stimulants s. 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 dose adjustment, then at least every 6 months and at every visit; discontinuation of treatment may be appropriate.

Psychotic or manic symptoms

Exacerbation of pre-existing psychotic or manic symptoms.

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

Treatment-emergent psychotic symptoms (visual/tactile/auditory hallucinations and delusions) or mania in children and adolescents without prior history of psychotic illness or mania may 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.

Bipolar disorder

Particular care should be taken in using dexamfetamine to treat ADHD in patients with comorbid bipolar disorder (including untreated type I bipolar disorder or other forms of bipolar disorder) based on potential expedite 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 anamnesis, including a family anamnesis 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 dose adjustment, then at least every 6 months and at every visit.

Aggressive or hostile behavior

The emergence or worsening of aggression or hostility may 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.

Tics

Dexamfetamine is associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette’s syndrome has also been reported. Family anamnesis 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 dose adjustment 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 dose

adjustment and then at least every 6 month or at every visit.

Growth

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

The effects of dexamfetamine on final height and final weight are still unknown and are currently being studied.

Growth should be monitored during dexamfetamine treatment: height, weight and appetite should be recorded at least 6 monthly by using 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 anamnesis 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.

Fatigue

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

Drug/Laboratory Test Interactions

This product contains dexamfetamine which may induce a positive laboratory test for amfetamines, particularly with an immunoassay screening test.
Amfetamines may cause a significant increase in plasma corticosteroid levels. This increase is greatest in the evening. Amfetamines may interfere with urinary steroid determination.

Renal or hepatic impairment

There is no experience with the use of dexamfetamine in patients with renal or hepatic impairment. In these patients peak plasma levels may be higher and elimination could be prolonged. Thus, dexamfetamine should be used with special caution in this patient group by careful titration of the dose.

Hematological 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.

Excipient: isomalt

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

4.5 Interaction with other medicinal products and other forms of interaction

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

Pharmacokinetic interactions

Serotonergic syndrome has rarely occurred in association with the use of amfetamines such as dexamfetamine when co-administered with serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin- and norepinephrine reuptake inhibitors (SNRIs).

Effects of other substances on the pharmacokinetics of dexamfetamine

It is not known to which extent the dexamfetamine metabolism is dependent on CYP enzymes. Co-administration of potent inhibitors or inducers of CYP enzymes should be made with caution.

Agents that lower blood levels of amfetamines

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

Urinary acidifying agents (ammonium chloride, sodium dihydrogen 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.

Agents that increase blood levels 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 efficacy of amfetamines.

Effects of dexamfetamine on the pharmacokinetics of other substances

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. *In vitro* data has shown that dexamfetamine may inhibit the transporters OCT1 and OCT2 (e.g. metformin). The clinical relevance of this is not known.

There are reports indicating that dexamfetamine may inhibit the metabolism of coumarin anticoagulants, antiepileptics (e.g. phenobarbital, phenytoin, and primidone) and some antidepressants (tricyclics and selective serotonin reuptake inhibitors). When initiating and terminating 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).

The absorption of antiepileptics (e.g. phenobarbital, phenytoin, primidone, and ethosuximide) may be delayed by dexamfetamine. The net effect of possible inhibition of metabolism and delayed absorption is not known.

Pharmacodynamic interactions

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 amfetamines

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 events. Due to a possible increase in blood pressure, special caution is advised if Dexatin is administered to patients being treated with vasoconstrictors (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.

Agents that may increase the effects of amfetamines

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

Agents that may reduce the effects of amfetamines
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 at concurrent administration of haloperidol.

Use with alcohol

Alcohol may exacerbate the CNS-related 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
Data from a cohort study of in total approximately 5570 pregnancies exposed to amfetamine in the first trimester do not suggest an increased risk of congenital malformation. Data from another cohort study in approximately 3100 pregnancies exposed to amfetamine 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 cause reproductive toxicity (see

section 5.3). The use of Dexatin during pregnancy is not recommended. Women of childbearing age should discontinue the use of Dexatin 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 Dexatin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
No human data on the effect of dexamfetamine on fertility are available.

4.7 Effects on ability to drive and use machines

Dexamfetamine may 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

Summary of the safety profile
Adverse reactions observed with dexamfetamine treatment reflect side effects commonly associated with stimulants. Very common and common adverse reactions include decreased appetite, weight loss, insomnia, dry mouth, headache, and upper abdominal pain.

Information on the frequency of these effects has been obtained from published clinical studies and meta-analyses.

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)

Organ class	**Very common (≥1/10)**	**Common (≥ 1/100, < 1/10)**	**Rare (≥ 1/10 000, < 1/1 000)**	**Very rare (< 1/10 000)**	**Frequency not known (cannot be estimated from the available data)**
Blood and lymphatic system disorders				Anaemia, leukopenia, thrombocytopenia, thrombocytopenic purpura	
Cardiac disorders		Arrhythmia, palpitations, tachycardia	Angina pectoris	Cardiac arrest	Cardiomyopathy, myocardial infarction
Congenital, familial, and genetic disorders				Tourette's syndrome	

Eye disorders			Impaired accommodation, blurred vision, mydriasis		
Gastrointestinal disorders		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			Ischaemic colitis, diarrhoea
General disorders and administration site conditions					Chest pain, hyperpyrexia, fatigue, sudden death (see section 4.4)
Hepatobiliary disorders				Abnormal liver function including hepatic enzyme elevations and hepatic coma	
Immune system disorders					Hypersensitivity including angioedema and anaphylaxis
Investigations		Changes in blood pressure and heart rate (usually increases)			
Metabolism and nutrition disorders	Decreased appetite, reduced weight gain and weight loss during prolonged use in children				Acidosis
Musculoskeletal and connective tissue disorders		Arthralgia	Growth retardation during prolonged use in children	Muscle cramps	Rhabdomyolysis

Nervous system disorders		Vertigo, dyskinesia, headache, hyperactivity	Fatigue	Muscle cramps, choreoathetoid movements, intracranial haemorrhage, 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.	Ataxia, dizziness, dysgeusia, concentration difficulties, hyperreflexia, stroke, tremor
Psychiatric disorders	Insomnia, nervousness	Abnormal behaviour, aggression, excitation, anorexia, anxiety, depression, irritability		Hallucinations, psychosis/psychotic reactions, suicidal behaviour (including completed suicide), tics, worsening of pre-existing tics.	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					Renal damage
Reproductive system and breast disorders					Impotence
Skin and subcutaneous tissue disorders			Rash, urticaria	Erythema multiforme, exfoliative dermatitis, fixed drug eruption	Sweating, alopecia
Vascular disorders				Cerebral vasculitis and/or occlusion	Cardiovascular collapse, Raynaud's phenomenon

A toxic hypermetabolic state, characterized 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 may 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 national reporting system listed in Appendix V

4.9 Overdose

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

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

Treatment
There is no specific antidote to amfetamine 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 or gastric lavage 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.

In case of amfetamine overdose, consult a poison control center for guidance or treat as clinically indicated. The prolonged duration of action of amfetamine should be considered when treating patients with overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychostimulants, agents used for ADHD and nootropics, centrally acting sympathomimetics ATC code: N06BA02

Mechanism of action
Dexamfetamine is a sympathomimetic amine with a central stimulant and anorectic activity. The mode of therapeutic action in attention deficit hyperactivity disorder (ADHD) is not fully established. Amfetamine is thought to block the reuptake of noradrenaline and dopamine into the presynaptic neuron and increase the release of these monoamines into the synaptic cleft.

Pharmacodynamic effects
Peripheral actions include elevations of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action. Neither there is specific evidence that clearly establishes the mechanism whereby amfetamines produce mental and behavioural effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system.

5.2 Pharmacokinetic properties

Absorption
Dexamfetamine is highly lipophilic and rapidly absorbed from the gastrointestinal tract. Following oral administration of dexamfetamine, maximal plasma concentration is achieved in approximately 2-4 hours.

Distribution
Dexamfetamine is highly liposoluble and cross blood-brain barrier following oral intake. The rate of protein binding of dexamfetamine is low and is approximately 20%. The apparent volume of distribution of dexamfetamine is between 4-5 L/kg.

Biotransformation
The biotransformation of amfetamine takes place in the liver to more hydrophilic components which may be more easily eliminated. The main metabolic pathway is hydroxylation on the side chain alpha-carbon, which is then deamined/conjugated and finally excreted as hippuric acid (inactive metabolite). Dexamfetamine can also be oxidized at the benzene ring to form para-hydroxyamfetamine and hydroxylated on the side chain beta-carbon to form norephedrine. These two metabolites are active, but account for a small part of the metabolism. CYP2D6 is involved with formation of 4-hydroxy-amfetamine.

Elimination
Dexamfetamine is primarily excreted in the urine and tubular reabsorption is relatively high due to its lipophilic properties. The elimination of dexamfetamine is pH-dependent, at low pH about 60% of the amfetamine is eliminated in the unaltered form within 48 hours and in alkaline urine, only 7% is eliminated. In children (5-12 years), the average plasma half-life (t½) of dexamfetamine is approximately 7 hours. The half-life is approximately 8-12 hours in healthy adults.

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, but only at doses 41 times the human dose. In rats treated with a dose corresponding to 12.5 times the human dose and rabbits treated with doses of dexamfetamine corresponding to up to 7 times the human dose no embryotoxic effects were observed.

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

Isomalt (E953)
Magnesium stearate (E470b)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Blister:
5 mg: 1 year
10 mg and 20 mg: 2 years

HDPE container:
5 mg: 18 months
10 mg: 21 months
20 mg: 2 years

6.4 Special precautions for storage

Blister:
5 mg and 20 mg: Do not store above 30°C.
10 mg: Do not store above 25°C.

HDPE container:
All strengths: Do not store above 30°C.

6.5 Nature and contents of container

All strengths: 10, 20, 30, 50 or 100 tablets in transparent PVC/PE/PVdC/Al-blisters.

All strengths: 28, 30, 50, 98 or 100 tablets in HDPE container with a child-resistant and round polypropylene screw cap with desiccant.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

<to be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)

<to be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

2026-06-24