NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Dexamfetamine Tablets, Tablet, 5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Name and strength of the active substance:
Dexamfetamine sulfate 5 mg

Excipient(s) with known effect:
Lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral – tablet

Presentation
White, 8 mm, normal convex tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the treatment of well-established and proven narcolepsy. It is also indicated for children with refractory hyperkinetic states under the supervision of a physician specialising in child psychiatry.

4.2. Dose and method of administration

Dexamfetamine should be started at the lowest possible dose and should then be individually and slowly adjusted to the lowest effective dose for each individual.

Time of administration should receive special attention because of insomnia.

For narcolepsy:

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

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

Children:

- *Children up to 6 years of age:*
  Dosage has not been established.

- *Children 6 to 12 years of age:*
  Oral, 5mg a day, the dosage being increased by 5 mg a day at one-week intervals until the desired response is obtained or until the adult dose is reached.

For attention-deficit hyperactivity disorders:

Where possible, drug administration should be interrupted occasionally to determine if there is an occurrence of behaviour symptoms sufficient to require continued therapy.

If therapy is recommenced after discontinuation, it should not be started at the dose that had been reached prior to treatment interruption but should be re-titrated from the usual starting dose.

Children:

- *Children up to 3 years of age:*
  Use is not recommended.

- *Children 3 to 5 years of age:*
  Oral, 2.5 mg once a day, the dosage being increased by 2.5 mg a day at one-week intervals until the desired response is obtained.

- *Children 6 years of age and over:*
  Oral, 5 mg one or two times a day, the dosage being increased by 5 mg a day at one-week intervals until the desired response is obtained.

4.3. Contraindications

Cardiac arrhythmia, patients with symptomatic cardiovascular disease including those with a history of myocardial infarction. Severe angina pectoris and ischaemic heart disease, moderate to severe hypertension, hyperthyroidism, phaeochromocytoma, known hypersensitivity or idiosyncrasy to dexamfetamine, sympathomimetic amines, or any of the excipients listed in section 6.1, glaucoma, porphyria, motor tics and Tourette syndrome.

Anxiety, tension, and agitation. Patients who currently exhibit severe depression, anorexia nervosa, hyperexcitability, psychotic symptoms or suicidal tendency.

Patients with known drug dependence or alcohol abuse.

Concurrent treatment with or within 14 days following the administration of mono amine oxidase inhibitors (hypertensive crises may result, see Section 4.5 Interactions with other medicines and other forms of interactions).

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

Pregnancy and breast-feeding mothers (see Section 4.6 Fertility, pregnancy and lactation).

4.4. Special warnings and precautions for use

Warning of drug abuse

Amfetamines have a high potential for drug abuse. Care should be exercised in the selection of patients for amfetamine therapy and prescription size should be limited to that required to achieve the therapeutic goal. Patients should be cautioned against increasing the recommended dosage. Should psychological dependence occur, gradual withdrawal of the medication is recommended. Abrupt cessation following prolonged high dosage results in extreme fatigue and mental depression; changes have also been noted on the sleep EEG. Manifestations of chronic intoxication with amfetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Pre-treatment assessment

Before starting treatment with dexamfetamine, it is important to consider the patient's personal and family cardiac and psychiatric history. In patients with identified or potential cardiovascular or psychiatric risk factors, further investigation or specialist review may be considered.

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

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

Children and adolescents

Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.

Adults

Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs.

It is essential that children, adolescents, or adults with pre-existing structural cardiac abnormalities or other serious heart problems being considered for treatment are assessed by a cardiologist before initiating treatment. Ongoing cardiological supervision should be maintained throughout treatment in these patients.

Hypertension and other cardiovascular disease

According to the FDA's voluntary Adverse Event Reporting System (AERS) database for the period January 1992 to February 2005, 7 of the 14 cases of sudden death in children and adolescents occurred during or shortly after exercise, or in association with hyperthermia and dehydration. However, exercise is almost universal in children, and this does not necessarily indicate a true association. Nevertheless, due to the effects on the sympathetic nervous system, dexamfetamine should be used with caution in patients who are involved in strenuous exercise or activities, use stimulants, or have a family history of sudden/cardiac death or life- threatening arrhythmia.

Dexamfetamine should be used with caution in patients with mild hypertension, and in such patients, blood pressure should be monitored more frequently than usual. Because dexamfetamine can increase blood pressure and heart rate, it is not recommended in patients with conditions which may be aggravated by an increase in blood pressure or heat rate.

Aggressive behaviour

Emergent aggressive behaviour or a worsening of baseline aggressive behaviour has been reported during stimulant therapy. However, patients with ADHD may experience aggression as part of their medical condition. Therefore, causal association with treatment is difficult to assess. Physicians should evaluate the need for adjustment of treatment regimen in patients experiencing these behavioural changes, bearing in mind that upwards or downwards titration may be appropriate.

Depression, bipolar disorders or psychosis

Administration of dexamfetamine may exacerbate symptoms of behaviour disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Prior to initiating treatment with dexamfetamine, patients with co-morbid 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.

In patients with a past history of or concurrent depression, bipolar disorder or psychosis, dexamfetamine should be used under close supervision and the patient should be closely observed for worsening of depression or the development of suicidal thoughts or behaviour, or thoughts or acts of self-harm. Treatment with dexamfetamine should be withdrawn in patients who develop suicidal ideation or behaviour, thoughts or acts of self-harm, psychosis/mania, or worsening of aggression/violent behaviour, and treatment should be re- introduced with caution following recovery.

Particular care should be taken in using dexamfetamine to treat ADHD in patients with co-morbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients.

Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania can be caused by dexamfetamine at usual doses.

Peripheral vasculopathy, including Raynaud's phenomenon

Stimulants, including dexamfetamine, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, have been observed in post-marketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

Seizures

There is some clinical evidence that dexamfetamine may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Long term suppression of growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children older than 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e. treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development.

Published data are inadequate to determine whether chronic use of dexamfetamine may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well. Therefore, growth should be monitored during treatment with dexamfetamine, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Motor tics or Tourette's syndrome

Use with caution in patients with a family history of motor tics or Tourette syndrome.

Regular review

Blood pressure, cardiovascular status and psychiatric status should be reviewed regularly during treatment with dexamfetamine. Children on dexamfetamine should have their growth monitored, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Use in renal impairment

Use with caution in renal insufficiency.

Use in the elderly
There is no information available on use in the elderly.

Paediatric use
Long term effects of amfetamines in children have not been well established and use in children under 3 years of age with attention deficit disorder with hyperactivity is not recommended (see Section 4.2 Dose and method of administration).

Infants born to mothers dependent on amfetamines have an increased risk of premature delivery and low birth weight. These infants may experience symptoms of withdrawal as demonstrated by dysphoria, including agitation and significant lassitude.

Effects on laboratory tests
Amfetamines can cause a significant elevation in plasma corticosteroid levels (this increase is greatest in the evening) and may interfere with urinary steroid determinations.

4.5. Interaction with other medicines 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 MAOIs 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.

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

Acute dystonia has been noted with concurrent administration of haloperidol. Haloperidol blocks dopamine and norepinephrine re-uptake, thus inhibiting the central stimulant effects of amphetamines.

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

Amphetamines potentiate the analgesic effects of meperidine (pethidine).

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

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

Medicines that affect noradrenaline levels should be used cautiously when co-administered with dexamfetamine because of the potential for additive or synergistic pharmacological effects.

The use of atomoxetine in patients taking amfetamines may lead to additive adverse effects, such as psychosis and movement disorders. The effects of amfetamines on mood and blood pressure may be reduced.

4.6. Fertility, pregnancy and lactation

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

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

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

Paediatrics: Prolonged administration of dexamfetamine sulfate to children may inhibit growth. Height and weight in children should be monitored. Psychotic children may experience exacerbation of symptoms of behaviour disturbance and thought disorder. It provokes or exacerbates motor and vocal tics and Tourette’s syndrome, necessitating

clinical evaluation before administration of dexamfetamine sulfate.

4.7. Effects on ability to drive and use machines

Dexamfetamine may affect ability to drive or operate machinery.

4.8. Undesirable effects

Cardiac disorders: cardiomyopathy, myocardial infarction, palpitations, tachycardia

Eye disorders: mydriasis, visual disturbance

Gastrointestinal disorders: abdominal cramps, colitis ischaemic, diarrhoea, dry mouth, nausea.

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

Investigations: blood pressure decreased, blood pressure increased

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

Musculoskeletal and connective tissue disorders: rhabdomyolysis

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

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

Renal and urinary disorders: renal damage

Reproductive system and breast disorders: impotence

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

Vascular disorders: cardiovascular collapse, cerebral vasculitis

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

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

retardation or agitation, anhedonia, and drug craving.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9. Overdose

Individual response to amfetamines varies widely. While toxic symptoms occasionally occur as an idiosyncrasy at dosages as low as 2 mg, they are uncommon with doses of less than 15 mg. Dosages of 30 mg can produce severe reactions, yet doses of 400 mg to 500 mg are not necessarily fatal.

Symptoms include dilated and reactive pupils, shallow rapid respiration, rhabdomyolysis, fever, chills, sweating, hyperactive tendon reflexes.

Central effects may include restlessness, aggressiveness, anxiety, confusion, delirium, hallucinations, panic attacks and suicidal or homicidal tendencies. The stimulant effect is usually followed by depression, lethargy, exhaustion.

Cardiovascular effects may include anginal pain, extrasystoles, and other arrhythmias, flushing, headache, hypertension, or hypotension, pallor, palpitations, tachycardia. Circulatory collapse and syncope may occur.

Gastrointestinal effects include nausea, vomiting, diarrhoea and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.

Drug abuse and dependence
Amfetamines have been extensively abused. Tolerance, extreme psychological dependence and severe social disability have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage results in extreme fatigue and mental depression; changes are also noted on sleep EEG.

Manifestations of chronic intoxication with amfetamines include restlessness, tremor, hyperreflexia, rhabdomyolysis, rapid respiration, hyperpyrexia, confusion, aggression, hallucinations, panic states, severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia. This is uncommon with oral amfetamines.

Treatment of acute intoxication
Treatments of overdoses are usually symptomatic. Emergency stabilization is required to manage those suffering seizure, cardiac arrest, or the acute consequences of arteriospasm or rupture such as stroke.

Efficacy has not been proven for the use of activated charcoal and should only be

considered in cases of life threatening overdoses. Activated charcoal may reduce absorption of the drug if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via nasogastric tube, once the airway is protected. In case of massive overdose, whole bowel irrigation (iso-osmotic polyethylene glycol electrolyte solution) may be beneficial, but is not otherwise recommended. Insufficient data is available to recommend the use of haemodialysis or peritoneal dialysis.
For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Actions Dexamfetamine, the dextrorotatory isomer of amphetamine, is an indirect-acting sympathomimetic amine with central stimulant and anorectic activity. It increases motor activity and mental alertness and diminishes drowsiness and a sense of fatigue. In children with attention-deficit hyperactivity disorder, dexamfetamine decreases motor restlessness and enhances the ability to pay attention. Amphetamine facilitates the action of dopamine and norepinephrine by blocking re-uptake from the synapse, inhibits the action of monoamine oxidase (MAO), and facilitates the release of catecolamines. It may also stimulate inhibitory autoreceptors in the *substantia nigra* and *ventral tegmentum*.

5.2. Pharmacokinetic properties

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

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

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

5.3. Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those included in other sections.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Acacia
Colloidal silicon dioxide

Lactose monohydrate
Magnesium stearate
Maize starch
Purified talc

6.2. Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3. Shelf life

24 months from date of manufacture stored at or below 25°C.

6.4. Special precautions for storage

Store below 25°C in an air-tight container. Protect from light. Do not refrigerate.

6.5. Nature and contents of container

Pack of 100 tablets in an amber glass bottle.

6.6. Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Class B1 Controlled Drug

8. SPONSOR

Noumed Pharmaceuticals Ltd
Auckland, New Zealand
Freephone 0800 527 545

9. DATE OF FIRST APPROVAL

31 December 1969

10. DATE OF REVISION OF THE TEXT

11 February 2025

SUMMARY TABLE OF CHANGES

Section changes	Summary of new information
8	Sponsor address updated.