NEW ZEALAND DATA SHEET

1. PRODUCT NAME (strength pharmaceutical form)

Aspen Dexamfetamine, Tablet, 5mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipient(s) with known effect: For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral tablet.

Presentation: White, round flat tablet with bevelled edges with “D5” imprinted and scored on one side and plain on the other.

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

For attention-deficit hyperactivity disorders:

Children:

Children up to 3 years of age
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.

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 restarted at the dose that had been reached prior to treatment interruption, but should be re-titrated from the usual starting dose.

4.3 Contraindications

Dexamfetamine sulfate tablets are contraindicated in patients with known hypersensitivity to dexamfetamine or other amfetamine derivatives or any of the excipients.

Do not use in patients with cardiac arrhythmia, patients with symptomatic cardiovascular disease including those with a history of myocardial infarction, severe angina pectoris, ischaemic heart disease and moderate to severe hypertension.

Do not use in patients with advanced arteriosclerosis.

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

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

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

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

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

Do not use during pregnancy (see section 4.6 Fertility, Pregnancy and Lactation).

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.

4.4 Special warnings and precautions for use

Motor tics:
Use with caution in patients with a family history of dystonias. If tics develop, discontinue treatment with dexamfetamine. Dexamfetamine is likely to reduce the convulsant threshold therefore caution is advised in patients with epilepsy.

Long term suppression of growth:
Height and weight should be carefully monitored in children as growth retardation may occur. Children who are not gaining weight as expected should have their treatment interrupted temporarily.

Use in renal impairment:
Caution should be used when administering dexamfetamine to patients with impaired kidney function or unstable personality.

Warning of drug abuse:
Amfetamines have a high potential for drug abuse. Drug dependence, with consumption of increasing doses to levels many times those recommended may occur as tolerance develops. At such levels, a psychosis which may be clinically indistinguishable from schizophrenia can occur. Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression; changes have also been noted on the sleep EEG.

Sudden death and pre-existing structural cardiac abnormalities or other serious heart problems:
Sudden death has been reported in association with the use of stimulants of the central nervous system at usual doses in children with structural cardiac abnormalities or other serious heart problems.

Although some structural cardiac abnormalities alone may carry an increased risk of sudden death, stimulant products are not recommended in children, adolescents, or adults with known structural cardiac abnormalities, 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 (see section 4.3 Contraindications).

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.

Cardiomyopathy has been reported with chronic amfetamine use.

Hypertension:
Blood pressure should be monitored at appropriate intervals in all patients taking dexamfetamine, especially those with hypertension. 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 heart 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.

Psychiatric adverse events:
Administration of stimulants may exacerbate symptoms of behaviour disturbance and thought disorders in patients with a pre-existing psychotic disorder.

Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.

Treatment emergent psychotic or manic symptoms, e.g. hallucinations, delusional thinking or mania in children or adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant and discontinuation of treatment may be appropriate.

Patients beginning treatment with stimulants for ADHD should be monitored for the appearance, or worsening of, aggressive behaviour or hostility.

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 milk; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, have been observed in postmarketing 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.

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.

Geriatrics:

No data is available on relationship of age to the effects of dexamfetamine in geriatric patients.

Other:

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

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

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

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

Phenothiazines may inhibit the actions of dexamfetamine.

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

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

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

Amfetamines potentiate the analgesic effects of meperidine (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 amfetamines. Urinary alkalizing agents (acetazolamide, some thiazides) increase the concentration of the non-ionized species of the amfetamine molecule, thereby decreasing urinary excretion. Both groups of agents increase blood levels and efficacy of amfetamines.

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

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

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 atomexetine 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 amfetamines 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 behavior, panic states, paranoia, psychosis/ psychotic reactions, restlessness, tics

Renal and urinary disorders: renal damage

Reproductive system and breast disorders: impotence

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

Vascular disorders: cardiovascular collapse, cerebral vasculitis

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

Cessation of, or reduction in, 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 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

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

coma, circulatory collapse and death.

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

Treatment of acute intoxication:
Treatments of overdoses are usually symptomatic.

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.

Excretion of dexamfetamine may be increased by forced acid diuresis.

Chlorpromazine antagonizes the central stimulant effects of amfetamines and can be used to treat amfetamine intoxication.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Actions:
Dexamfetamine, the dextrorotatory isomer of amfetamine, 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. Amfetamine 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

Lactose monohydrate
Wheat starch
Povidone
Magnesium stearate

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.

6.4 Special precautions for storage

Store below 25^{o}C.

6.5 Nature and contents of container

Pack of 100 tablets in a HDPE 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

Pharmacy Retailing (NZ) Limited
58 Richard Pearse Drive
Airport Oaks
AUCKLAND

9. DATE OF FIRST APPROVAL

13 October 2022

10. DATE OF REVISION OF THE TEXT

19 April 2023

SUMMARY TABLE OF CHANGES

Section changes	Summary of new information
4.2, 4.3, 4.4, 4.5 & 4.9	Safety update to align with the Australian product information, as requested by Medsafe.