SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

MINEX 15 mg capsule

MINEX 30 mg capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each MINEX capsule contains phentermine hydrochloride, equivalent to either 15 mg or 30 mg phentermine and are sugar-free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard gelatin capsules.

MINEX 15 mg**:** Size ‘3’ hard gelatin capsule with white opaque cap and grey opaque body, imprinted with ‘PT’ on cap and ‘15’ on body in black ink and containing brown to light brown coloured spherical beads.

MINEX 30 mg: Size ‘3’ hard gelatin capsule with purple cap and grey opaque body, imprinted with ‘PT’ on cap and ‘30’ on body in white ink and containing brown to light brown coloured spherical beads.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MINEX is a medicine used for the management of obesity and is classified as an anorectic medicine.

MINEX is a short-term adjunct in a medically monitored comprehensive regimen of weight reduction. This is based, for example, on diet (calorie/kilojoule restriction), exercise, and modification of behaviour in obese patients with a body mass index (BMI) of at least 30 kg/m^2 or higher and who have not achieved an adequate clinical response to a suitable weight-reducing regimen alone.

In patients with a lower BMI with other risk factors, treatment with MINEX can be initiated. Before prescribing MINEX secondary organic causes of obesity should be excluded.

4.2 Posology and method of administration

Adults and Children over 12 years:

Take one capsule daily at approximately 7 a.m., swallowed whole. A dose in the evening should be avoided, as MINEX may induce insomnia.

It is recommended that treatment should be initiated under the care of a medical practitioner experienced in the treatment of obesity.

The recommended dose of MINEX should not be exceeded, and MINEX should not be combined with other appetite suppressants, to increase the effect.

Patients require medical review after a defined course of treatment, which ideally should

not exceed three months.

Paediatric population

Children under 12 years:

MINEX is not recommended for children under 12 years old.

Method of administration

MINEX capsules are for oral use.

MINEX are to be swallowed whole.

4.3 Contraindications

- Hypersensitivity to phentermine and sympathomimetic medicines or to any of the ingredients of MINEX
- Pulmonary artery hypertension, arterial hypertension, cerebrovascular disease
- Cardiac disease including dysrhythmias, advanced arteriosclerosis
- Hyperthyroidism
- Agitated states or a history of psychiatric disorders including anorexia nervosa and depression
- Glaucoma
- History of drug/alcohol abuse or dependence
- Obstructive uropathy
- Poorly controlled epilepsy
- Concomitant treatment with Monoamine Oxidase (MAO) Inhibitors or within 14 days

following their administration

- Pregnancy and lactation
- Children under 12 years old.

4.4 Special warnings and precautions for use

Concomitant medicine:

MINEX is only indicated as a short-term (a few weeks) monotherapy for the exogenous obesity management. The safety and efficacy of combination therapy with MINEX and any other medicine for weight loss (including prescribed medicine, over-the-counter medicine and herbal products) have not been established. Consequently, co-administration with additional medicines for weight loss is not recommended.

Since the selective serotonin reuptake inhibitors (e.g. sertraline, fluoxetine, paroxetine, fluvoxamine), ergot-like medicines and clomipramine affect serotonin metabolism - there is a risk that the combination of these medicines with MINEX can be associated with cardiac valvular disease.

Valvular Heart Disease:

Serious regurgitant cardiac valvular disease, primarily affecting the aortic, mitral and/or tricuspid valves, has been described in otherwise healthy individuals who took a combination of MINEX with fenfluramine or dexfenfluramine for weight loss. The accuracy of the etiology of these valvulopathies has not been established and their course in persons after the medicine use were stopped is not fully known.

Primary Pulmonary Hypertension (PPH):

PPH is a rare, frequent fatal lung disease. Cases of primary pulmonary hypertension have been described in patients who have received MINEX.

The primary symptom of PPH is usually dyspnoea. Other early symptoms include: angina pectoris, syncope, lower extremity oedema or the unexplained start or aggravation of diminished exercise tolerance.

Under these circumstances, treatment should be immediately discontinued, and the patient referred to a specialist unit for investigation.

PPH has been reported in patients who received a combination of phentermine with fenfluramine or dexfenfluramine.

Hypertension and kidney impairment:

In patients with mild hypertension and kidney impairment MINEX should be used with caution. It is recommended to determine that there is no loss of blood pressure control in the first days of treatment with MINEX.

Epileptic patients:

Use MINEX with caution in epileptic patients.

Diabetic patients:

In patients receiving MINEX, response to insulin and oral hypoglycaemic medicines may vary due to changes in dietary regimes. This should be kept in mind if MINEX is used in diabetic patients.

Inappropriate use:

Inappropriate use has been reported with similar medicines and the possibility of this occurrence should be considered with MINEX.

Cardiac and cerebrovascular accidents:

Infrequent cases of cerebrovascular and cardiac events have been described, often after rapid weight loss. Special care should be taken to ensure gradual and controlled weight loss in obese patients, who are at risk to develop vascular disease. In patients under treatment with anti-hypertensive medicines, MINEX should be used with caution since it may cause loss of blood pressure control. This is also true in patients receiving psychotropic medicines, including sedatives and sympathomimetic medicines.

Development of tolerance, discontinuation in case of tolerance

If a tolerance to the anorectant effect develops, the recommended dosage should not be exceeded to increase the effect. It is recommended that the medicine should be discontinued.

4.5 Interaction with other medicines and other forms of interaction

Monoamine Oxidase Inhibitors:

Monoamine oxidase inhibitors potentiate the effects of MINEX (see section 4.3) and may result in a hypertensive crisis and is thus contraindicated during or within 14 days after the administration of monoamine oxidase inhibitors.

Sympathomimetic medicines:

MINEX should be used with caution in patients receiving sympathomimetic medicines as phentermine is an indirect-acting sympathomimetic which may interact with other medicine.

Adrenergic neurone blocking medicines:

MINEX antagonises adrenergic neurone blocking medicines such as clonidine, methyldopa and guanethidine and may decrease their hypotensive effect.

Alcohol

Concomitant use of alcohol with phentermine may result in an adverse drug reaction.

Insulin and oral hypoglycemic medication

Requirements may be altered (see section 4.4).

Selective serotonin reuptake inhibitors, ergot-like medicines and clomipramine:

Selective serotonin reuptake inhibitors (e.g. fluoxetine, sertraline, fluvoxamine, paroxetine), ergot-like medicines and clomipramine (see section 4.4).

4.6 Fertility, pregnancy and lactation

MINEX is contradicted in pregnancy and lactation.

Pregnancy

Due to inadequate evidence of safety in human pregnancy, MINEX should not be used in pregnant women.

Studies in animals have shown evidence of an increased occurrence of foetal damage.

Breastfeeding

There are no data available on the safety of MINEX in lactation and as such, its use in lactating women should be avoided.

Fertility

There is no information on the potential for MINEX to impair fertility in humans.

4.7 Effects on ability to drive and use machines

MINEX may impair the ability to perform activities requiring mental alertness, such as driving and operating machinery, and patients therefore should be cautioned accordingly.

4.8 Undesirable effects

Summary of the safety profile

Serious adverse reactions including primary pulmonary hypertension (symptoms include, dyspnoea, angina pectoris, syncope, lower extremity oedema, unexplained onset or aggravation of diminished exercise tolerance) require immediate discontinuation of MINEX and further investigation under specialist care.

Tabulated list of adverse effects

System Organ Class	**Frequency**	**Side effects**
Psychiatric disorders	Frequency unknown	Psychosis
Nervous system disorders	Frequent Less frequent	Overstimulation, restlessness, nervousness, insomnia, tremor, dizziness, headache Euphoria which may be followed by fatigue and depression, psychotic episodes, hallucinations, dysphoria
Eye disorders	Frequency unknown	Blurred vision
Cardiac disorders	Frequent Frequency unknown	Tachycardia, palpitations, hypertension, precordial pain Myocardial infarction, cardiac failure, cardiac arrest, ischaemic events
Vascular disorders	Frequency unknown	Cardiovascular or cerebrovascular accidents, primary pulmonary hypertension (symptoms include, dyspnoea, angina pectoris, syncope, lower extremity oedema, unexplained onset or aggravation of diminished exercise tolerance), facial oedema, regurgitant vulvular heart disease, elevation of blood pressure
Gastrointestinal disorders	Frequency unknown	Nausea, vomiting, dry mouth, abdominal cramps, unpleasant taste, diarrhoea, constipation
Skin and	Frequency	Rash, urticaria

subcutaneous tissue disorders	unknown	
Renal and urinary disorders	Frequency unknown	Micturition disturbances
Reproductive system and breast disorders	Frequency unknown	Impotence, changes in libido

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 to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Signs and symptoms:

Irritability, rapid respiration, agitation, euphoria, restlessness, hyperreflexia, disorientation and tremor, aggressiveness, hallucinations and panic states may occur, followed by cardiac dysrhythmias, convulsions, fatigue, central nervous system depression and coma. Cardiovascular effects include hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhoea and abdominal cramps.

Management of overdose:

Treatment is largely symptomatic. The stomach should be emptied by emesis or stomach tube and washed out with water if the preparation has been ingested within the last three or four hours.

Provided renal function is adequate, elimination of phentermine has been shown to be assisted by acidification of the urine.

There is insufficient experience to recommend haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Centrally acting anti-obesity products

ATC code: A08AA01

Pharmacological classification: A 11.3 Anorexigenics

Phentermine is a sympathomimetic amine chemically related to amphetamine, with significant anorectic activity in animal models.

Its appetite suppressant effect is generally considered to be exerted through the hypothalamus, but it is not certain that this is the only effect related to weight loss.

The cardiovascular effects include a pressor response and increase in heart rate and force of contraction.

5.2 Pharmacokinetic properties

Absorption:

Phentermine is readily absorbed from the gastro-intestinal tract.

Following the administration of phentermine, phentermine reaches peak concentrations (C_{max}) after 3 – 4,4 hours.

Biotransformation:

The half-life of phentermine is about 25 hours. In one study in volunteer's acidification of the urine reduced the half-life to 7 – 8 hours.

Elimination:

Following an oral dose of phentermine capsule, one study demonstrated urinary excretion of unchanged medicine ranging from 62,7 % to 84,8 % in 72 hours. The remainder is metabolised in the liver.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:

Magnesium stearate

Sodium polystyrene sulfonate

***15 mg Gelatin capsule shell*:**

Gelatin

Iron oxide black

Titanium dioxide

30 mg Gelatin capsule shell:

Brilliant blue FCF

Erythrosin

Gelatin

Iron oxide black

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at or below 25 °C.

Keep blisters in carton until required for use.

6.5 Nature and contents of container

Clear plastic and plain aluminium foil blister strips containing 30 capsules in a carton.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

8. REGISTRATION NUMBERS

MINEX 15 mg: A53/11.3/0713

MINEX 30 mg: A53/11.3/0714

9. DATE OF FIRST AUTHORISATION

16 August 2022

10. DATE OF REVISION OF THE TEXT