PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

DYNA PENTOXIFYLLINE 400 mg SR, film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each DYNA PENTOXIFYLLINE 400 mg SR film coated tablet contains pentoxifylline 400 mg.

Each slow release film coated tablet contains sugar (lactose monohydrate, 31,34 mg).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Slow release film coated tablet.

Pink, oval film coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Symptomatic relief of intermittent claudication, associated with chronic occlusive arterial disorders of the limbs and trophic ulcers. Pentoxifylline may improve function as well as provide symptomatic relief.

- Raynaud's syndrome.

4.2 Posology and method of administration

Unless otherwise prescribed by a doctor, the usual dose is one DYNA PENTOXIFYLLINE 400 mg SR film coated tablet taken two to three times daily.

Special populations

Renal impairment

In patients with impairment of renal function (creatinine clearance below 30 mL/min) a dose reduction of approximately 30 % to 50 % may be necessary (see sections 4.4 and 5.2).

Hepatic impairment

A dose reduction is necessary in patients with severely impaired liver function (see sections 4.4 and 5.2).

Hypotension

Treatment should be started at low dose levels in hypotensive patients or patients whose circulation is unstable as well as in patients who would be at particular risk from a reduction in blood pressure (e.g., patients with severe coronary heart disease or relevant stenosis of blood vessels supplying the brain); in such cases, the dose must be increased gradually.

Paediatric population

DYNA PENTOXIFYLLINE 400 mg SR is not indicated for use in children as safety and efficacy have not been established in this patient group.

Method of administration

DYNA PENTOXIFYLLINE 400 mg SR should be taken after meals, swallowed whole with sufficient amounts of liquid (approximately half a glass).

Mothers on DYNA PENTOXIFYLLINE 400 mg SR should not breastfeed (see section 4.6).

Missed dose:

Doctors should advise patients who forget to take DYNA PENTOXIFYLLINE 400 mg SR to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- hypersensitivity to pentoxifylline or other methyl xanthines or any of the ingredients of DYNA PENTOXIFYLLINE 400 mg SR
- cerebral haemorrhage, extensive retinal haemorrhage, severe cardiac dysrhythmias and acute myocardial infarction
- porphyria
- pregnancy and lactation.

4.4 Special warnings and precautions for use

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At the first signs of an anaphylactic/anaphylactoid reaction, DYNA PENTOXIFYLLINE 400 mg SR must be discontinued immediately, and a physician must be informed.

DYNA PENTOXIFYLLINE 400 mg SR should be used with caution in patients with severe cardiac dysrhythmias, myocardial infarction, ischaemic heart disease or hypotensive patients.
DYNA PENTOXIFYLLINE 400 mg SR may potentiate the effect of antihypertensive medicines (see section 4.5).

Use with caution in patients with cirrhosis. Particularly careful monitoring is required in patients with severely impaired renal function (creatinine clearance below 30 mL/min). The dose of DYNA PENTOXIFYLLINE 400 mg SR may need to be adjusted in renal and hepatic impaired patients.

Use with caution in patients with an increased bleeding tendency such as anticoagulant medicine or coagulant disorders. Events of bleeding (e.g., skin mucosa) have been reported in patients treated with pentoxifylline with and without anticoagulants or platelet aggregation inhibitors. The serious cases are predominantly concentrated in the gastrointestinal, genitourinary, multiple site and surgical wound areas and are associated with bleeding risk factors. Thrombocytopenia has occurred.

Reports of aseptic meningitis were predominantly in patients with underlying connective tissue disorders.

High parenteral doses of DYNA PENTOXIFYLLINE 400 mg SR may enhance the hypoglycaemic action of insulin in diabetic patients (see section 4.5).

DYNA PENTOXIFYLLINE 400 mg SR should not be given concomitantly with ketorolac as there is reported to be an increased risk of bleeding and/or prolongation of the prothrombin time.

Careful monitoring is required in patients treated concomitantly with ciprofloxacin (see section 4.5).

Careful monitoring is required in patients treated concomitantly with theophylline (see section 4.5).

Information on excipients of DYNA PENTOXIFYLLINE 400 mg SR

DYNA PENTOXIFYLLINE 400 mg SR contains lactose. Patients with the rare hereditary conditions of lactose or galactose intolerance e.g., galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption should not take DYNA PENTOXIFYLLINE 400 mg SR.
DYNA PENTOXIFYLLINE 400 mg SR contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.
lactose or galactose intolerance.

4.5 Interaction with other medicines and other forms of interaction

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DYNA PENTOXIFYLLINE 400 mg SR has been shown to intensify hypoglycaemic action of insulin and oral hypoglycaemic medicines (see section 4.4). However, no effect on insulin release has been observed following administration of DYNA PENTOXIFYLLINE 400 mg SR.
It is recommended that patients using medicine to treat diabetes mellitus be carefully monitored.

Cases of increased anti-coagulant activity have been reported in patients concomitantly treated with DYNA PENTOXIFYLLINE 400 mg SR and anti-vitamin K. Monitoring of anti-coagulant activity in these patients is recommended when DYNA PENTOXIFYLLINE 400 mg SR is introduced, or the dose is changed.

DYNA PENTOXIFYLLINE 400 mg SR may potentiate the effect of anti-hypertensive medicines and the dosage of the latter may need to be reduced.

DYNA PENTOXIFYLLINE 400 mg SR should not be given concomitantly with ketorolac or meloxicam as there is an increased risk of bleeding and/or prolongation of prothrombin time.

Concomitant administration of DYNA PENTOXIFYLLINE 400 mg SR and theophylline may increase theophylline levels in some patients. Therefore, there may be an increase in and intensification of the adverse effects of theophylline.

Concomitant administration of DYNA PENTOXIFYLLINE 400 mg SR and cimetidine, may increase the average steady state plasma concentrations of pentoxifylline, as in DYNA PENTOXIFYLLINE 400 mg SR, and the active metabolite lisofylline.

Concomitant administration of DYNA PENTOXIFYLLINE 400 mg SR with ciprofloxacin may increase the serum concentration of pentoxifylline in some patients. Therefore, there may be an increase in, and intensification of adverse reactions associated with co-administration.

Because of the increased risk of bleeding, the concomitant administration of a platelet aggregation inhibitor (such as clopidogrel, eptifibatide, tirofiban, epoprostenol, iloprost, abciximab, anagrelide, NSAIDs other than selective COX-2 inhibitors, acetylsalicylates (ASA/LAS), ticlopidine, dipyridamole) with DYNA PENTOXIFYLLINE 400 mg SR should be undertaken with caution.

4.6 Fertility, pregnancy and lactation

Pregnancy

DYNA PENTOXIFYLLINE 400 mg SR is contraindicated in pregnancy as safety has not been established (see section 4.3).

Breastfeeding

Pentoxifylline passes into breast milk. DYNA PENTOXIFYLLINE 400 mg SR is contraindicated in breastfeeding as safety has not been established (see section 4.3).

4.7 Effects on ability to drive and use machines

DYNA PENTOXIFYLLINE 400 mg SR can cause side effects such as dizziness.

During DYNA PENTOXIFYLLINE 400 mg SR administration, patients should be cautioned about engaging in activities requiring rapid and precise responses such as driving a vehicle or operating machinery.

4.8 Undesirable effects

Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Side effects**
Blood and lymphatic system disorders	Less frequent Frequency unknown	Thrombocytopenia Leukopenia/neutropenia
Immune system disorders	Less frequent	Hypersensitivity reaction, anaphylactic/anaphylactoid reaction such as angioedema, bronchospasm and shock
Psychiatric disorders	Less frequent	Agitation, sleep disorder
Nervous system disorders	Less frequent	Dizziness, headache, aseptic meningitis*
Cardiac disorders	Less frequent	Palpitations, cardiac dysrhythmias, angina, tachycardia, angina pectoris
Vascular disorders	Less frequent	Hypotension, haemorrhage**
Respiratory, thoracic and mediastinal disorders	Less frequent	Bronchospasm

Gastrointestinal disorders	Frequent Frequency unknown	Nausea, epigastric discomfort, abdominal distension, vomiting, diarrhoea, gastric pressure, fullness, Hyper salivation
Hepatobiliary disorders	Less frequent	Cholestasis
Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Flushing, pruritus, erythema, urticaria, hot flushes Rash
Investigations	Less frequent	Transaminases increased

* See aseptic meningitis warning under section 4.4.

** See bleeding warning under section 4.4.

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 online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

Initial symptoms of acute overdose with DYNA PENTOXIFYLLINE 400 mg SR may be nausea, dizziness, tachycardia or hypotension. Furthermore, signs such as fever, agitation, flushing, loss of consciousness, areflexia, tonic-clonic convulsions and coffee ground vomiting as a sign of gastro-intestinal bleeding may occur. No specific antidote is known.

Management of overdose:

In addition to general measures for the management of poisoning, blood pressure should be closely monitored. A drip infusion of a plasma expander should be applied if there is a severe drop in blood pressure. An adequate airway must be maintained. Convulsions can be controlled with diazepam. Particular attention to supporting the cardiovascular system is required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Peripheral vasodilators

ATC code: C04AD03

Pharmacological classification: A.8 Medicines acting on the blood and haemopoietic system.

Mechanism of action

Pentoxifylline improves erythrocyte flexibility, microcirculatory flow, tissue oxygen concentrations and reduces viscosity.

5.2 Pharmacokinetic properties

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Absorption:

Pentoxifylline is readily absorbed from the gastrointestinal tract. Administration of pentoxifylline with food delays absorption and reduces peak plasma levels.

Biotransformation:

Pentoxifylline undergoes first-pass hepatic metabolism. Some metabolites are active.

Elimination:

The half-life of absorption of pentoxifylline is 4-6 hours. The apparent plasma half-life of pentoxifylline is reported to be 0,4 to 0,8 hours; that of the metabolites varies from 1,0 to 1,6 hours. In 24 hours 60 % of a single 400 mg dose is excreted in the urine mainly as metabolites

and less than 4 % is recovered as unchanged pentoxifylline in the faeces.

Pharmacokinetics in special patient groups

Elderly:

Elimination of pentoxifylline is decreased in elderly patients, with resulting increased potential for toxicity. In addition, elderly patients are more likely to have age-related renal function impairment, which may require caution in patients receiving pentoxifylline.

Hepatic impairment:

The elimination half-life of pentoxifylline and its metabolites is significantly prolonged in patients with hepatic cirrhosis (see sections 4.2 and 4.4).

Renal impairment:

Some metabolites have a prolonged half-life and accumulation may occur in patients with severe renal impairment (creatinine clearance less than less than 30 mL/min) who receive more than 400 mg once or twice daily (see sections 4.2 and 4.4).

Pregnancy:

Pentoxifylline and its metabolites cross into breast milk (see section 4.6).

Doses should be taken with meals to reduce gastrointestinal disturbances.

5.3 Preclinical safety data

Nothing of clinical relevance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet cores

Carnauba wax

Hypromellose 5 cps

Lactose monohydrate

Magnesium stearate

Purified stearic acid

Film coating

Cellulose acetate

Triacetin

Opadry II pink Y30-14132-AD (consisting of erythrosine dye (E127), hydroxypropylmethylcellulose, indigo carmine lake (E132), lactose monohydrate, titanium dioxide (E171) and triacetin)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the container well closed. Keep the blister in the outer carton until required for use.

6.5 Nature and contents of container

White polypropylene securitainer with a white polyethylene tear-tab cap, a foam insert and silica gel sachet containing 30 or 100 tablets.

Carton containing 30 or 100 tablets in blisters. Each blister comprises of white opaque PVC film coated with PVDC / Aluminium foil coated with PVDC.

Not all pack types and sizes are marketed.

6.6 Special precautions for disposal

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 NUMBER(S)

A36/8/0282

9. DATE OF FIRST AUTHORISATION

Date of registration: 11 December 2004

10. DATE OF REVISION OF THE TEXT

15 December 2022

NAM NS2 08/8/0183