SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pentoxifylline 400 mg modified release tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Pentoxifylline 400 mg

3 PHARMACEUTICAL FORM

Modified release tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Pentoxifylline is indicated in the treatment of peripheral vascular disease, including intermittent claudication and rest pain.

4.2 Posology and method of administration

Posology

Adults
The recommended initial dose is 1 tablet (400 mg) three times daily; two tablets daily may prove sufficient in some patients, particularly for maintenance therapy.

Elderly
No special dosage requirements.

Paediatric population
Pentoxifylline is not suitable for use in children.

Renal Impairment
In patients with impairment of renal function (creatinine clearance below 30ml/min) a dose reduction by approximately 30% to 50% may be necessary guided by individual tolerance.

Method of administration

Oral administration. Tablets should be taken with or immediately after meals, and swallowed whole with plenty of water.

4.3 Contraindications

Hypersensitivity to the active substance(s), other methylxanthines or to any of the excipients listed in section 6.1.

Also in patients with cerebral haemorrhage, extensive retinal haemorrhage, acute myocardial infarction and severe cardiac arrhythmias.

4.4 Special warnings and precautions for use

At the first signs of an anaphylactic/anaphylactoid reaction, Pentoxifylline must be discontinued immediately, and a physician must be informed.

Particular careful monitoring is required:

- In patients with hypotension or severe coronary artery disease, Pentoxifylline should be used with caution, as a transient hypotensive effect is possible and, in isolated cases, might result in a reduction in coronary artery perfusion.
- In patients with impaired renal function. In patients with a creatinine clearance of less than 30 ml/min it may be necessary to reduce the daily dose of Pentoxifylline to one or two tablets to avoid accumulation. In patients with severely impaired liver function the dosage may need to be reduced.
- In patients treated concomitantly with pentoxifylline and anti-vitamin K or platelet aggregation inhibitors (see also section 4.5).
- In patients treated concomitantly with pentoxifylline and antidiabetic agents (see also section 4.5).
- In patients treated concomitantly with pentoxifylline and ciprofloxacin (see also section 4.5).
- In patients treated concomitantly with pentoxifylline and theophylline (see also section 4.5).

Excipient(s) with known effect

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium- free'.

4.5 Interaction with other medicinal products and other forms of interaction

High doses of Pentoxifylline injection have been shown, in rare cases, to intensify the hypoglycaemic action of insulin and oral hypoglycaemic agents. However, no effect on insulin release has been observed with Pentoxifylline following oral administration. It is recommended that patients under medication for diabetes mellitus be carefully monitored.

Post-marketing cases of increased anti-coagulant activity have been reported in patients concomitantly treated with pentoxifylline and anti-vitamin K. Monitoring of anti-coagulant activity in these patients is recommended when pentoxifylline is introduced or the dose is changed.

Pentoxifylline may potentiate the effect of anti-hypertensive agents and the dosage of the latter may need to be reduced.

Pentoxifyllineshould not be given concomitantly with ketorolac as there is increased risk of bleeding and/or prolongation of prothrombin time.

Concomitant administration of pentoxifylline and theophylline may increase theophylline levels in some patients. Therefore there may be an increase in and intensification of adverse effects of theophylline.

Concomitant administration 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.

Potential additive effect with platelet aggregation inhibitors: 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 pentoxifylline should be undertaken with caution.

Concomitant administration with cimetidine may increase the plasma concentration of pentoxifylline and the active metabolite, lisofylline.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no information on the use of Pentoxifylline in pregnancy, but no untoward effects have been found in animal studies. Pentoxifylline should not be administered during pregnancy.

Breast-feeding
Pentoxifylline passes into breast milk in minute quantities. Because insufficient experience has been gained, the possible risks and benefits must be weighed before administration of Pentoxifylline to breast feeding mothers.

4.7 Effects on ability to drive and use machines

No effect known.

4.8 Undesirable effects

These adverse reactions have been reported in clinical trials or post-marketing. Frequencies are unknown.

System Organ Class	**Adverse Reaction**
Investigations	Transaminases increased
Cardiac disorders	Arrhythmia, Tachycardia, Angina Pectoris
Blood and lymphatic system disorders	Thrombocytopenia, Leukopenia/neutropenia
Nervous system disorders	Dizziness, headache, meningitis aseptic*
Gastrointestinal disorders	Gastrointestinal disorder, Epigastric discomfort, Abdominal distension, Nausea, Vomiting, Diarrhoea, Constipation, Hypersalivation
Skin and subcutaneous tissue disorders	Pruritus, Erythema, Urticaria, Hot flush, Rash

Vascular disorders	Haemorrhage**, Hypotension
Immune system disorders	Anaphylactic reactions, Anaphylactoid reaction, Angioedema
Hepatobiliary disorders	Cholestasis
Psychiatric disorders	Agitation, Sleep disorder
Respiratory disorders	Bronchospasm

Description of selected adverse reactions
* Reports of aseptic meningitis were predominantly in patients with underlying connective tissue disorders

** A few very rare 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. A causal relationship between Pentoxifylline therapy and bleeding has not been established. Thrombocytopenia has occurred in isolated cases.

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 professional are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose
The treatment of overdosage should be symptomatic with particular attention to supporting the cardiovascular system.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Purine derivatives, ATC code: C04AD03

Leukocyte properties of haemorrheologic importance have been modified in animal and in vitro human studies. Pentoxifylline has been shown to increase leukocyte deformability and to inhibit neutrophil adhesion and activation.

5.2 Pharmacokinetic properties

The half-life of absorption of Pentoxifylline is 4 – 6 hours. Pentoxifylline is extensively metabolised, mainly in the liver. Sixty percent of a single dose of Pentoxifylline is eliminated via the kidney over 24 hours.

5.3 Preclinical safety data
Nothing of clinical relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxyethyl cellulose, povidone, talc, magnesium stearate, hypromellose, macrogol 8000, erythrosine (E127). titanium dioxide (E171).

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Amber glass bottle: 100 or 250 tablets.
Plastic (PE) pots: 100 or 250 tablets.
Blister Pack (Alu/PVC): 10 or 90 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 49718/0108

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11/12/2023