PENTOXIFYLLINE EXTENDED RELEASE TABLETS 400MG
TAJ PHARMA

1. NAME OF THE MEDICINAL PRODUCT

Pentoxifylline Extended Release Tablets 400mg Taj Pharma

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

a) Each film coated tablet contains:

Pentoxifylline USP	400mg
Excipients	q.s.

3. PHARMACEUTICAL FORM

Tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pentoxifylline 400 is indicated in the treatment of peripheral vascular disease, including intermittent claudication and rest pain.

4.2 Posology and method of administration

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

Elderly: No special dosage requirements.

Children: Pentoxifylline 400 is not suitable for use in children.

Special Cases: 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.

4.3 Contraindications

Pentoxifylline 400 is contra-indicated in cases where there is known hypersensitivity to the active constituent, pentoxifylline other methyl xanthines or any of the excipients. 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 400 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 400 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.

Particularly careful monitoring is required 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 400 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).

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

Pentoxifylline 400 should 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 Pregnancy and lactation

There is no information on the use of Pentoxifylline in pregnancy but no untoward effects have been found in animal studies. Pentoxifylline 400 should not be administered during pregnancy.

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 400 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.

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

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 400 is 4-6 hours. Pentoxifylline is extensively metabolised, mainly in the liver. Sixty percent of a single dose of Pentoxifylline 400 is eliminated via the kidney over 24 hours.

5.3 Preclinical safety data

Nothing of clinical relevance.

6. PHARMACEUTICAL PARTICULARS

a) Each film coated tablet contains:

Pentoxifylline USP	400mg
Excipients	q.s.

6.1 List of excipients

Hydroxyethyl cellulose, povidone, talc, magnesium stearate, hypromellose, macrogol 8000, erythrosine. titanium dioxide.

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
PVC/PVDC/Al blisters.

Pack sizes: Blisters: 7, 14, 28, 30, 50, 90, 100 and 500mg modified-release tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
None.

7. MANUFACTURED IN INDIA BY:

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