For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

This package insert is continually updated. Please read carefully before using a new pack

Trental®

Pentoxifylline Prolonged-release Tablets IP

DESCRIPTION
Active Ingredient
Pentoxifylline

Therapeutic or Pharmacological Class
Haemorheologic agent

Pharmaceutical Form(s)
Prolonged-release film coated tablets

Composition
Trental 400
Each film coated Prolonged -release tablet contains Pentoxifylline I.P. 400 mg
Excipients…….q.s
Colour : Erythrosine
Indications

- Peripheral arterial occlusive disease (PAOD) of arteriosclerotic or diabetic origin (e.g., with intermittent claudication and rest pain).
- Trophic lesions (e.g., leg ulcers and gangrene)
- Cerebral vascular disease.
- Circulatory disturbances of the eye in conjunction with degenerative vascular disorders.

DOSAGE AND ADMINISTRATION
General

In principle, dosage, and mode of administration (oral or i.v.) is based on the type and severity of the circulatory disorders and on how the individual patient tolerates the drug. Dosage is generally based on the following guidelines:

- **PAOD Stage II (intermittent claudication) and circulatory disturbances of the eye; to start treatment or in support of oral therapy**

It is recommended that an infusion of 100 to 600 mg pentoxifylline be given once or twice daily.
It is recommended that pentoxifylline infusion be administered in a suitable infusion solution; depending on the accompanying diseases (e.g. congestive heart failure), it may be necessary to keep the infusion volume small. In such circumstances, in particular, a controlled volume infusion pump may be useful.

When low-dose infusion therapy is combined with oral therapy, the recommended total daily dose is 1200 mg pentoxifylline (intravenous plus oral).

For follow-on treatment, therapy may be continued with oral pentoxifylline alone.

- **PAOD Stages III and IV**

It is recommended that a total daily dose of 1200 mg pentoxifylline be administered in a suitable carrier solution either as a continuous infusion over a period of 24 hours, or as an infusion of 600 mg each given twice daily over periods of at least six hours.

Depending on the accompanying diseases (e.g. congestive heart failure), it may be necessary to keep the infusion volume small. In such circumstances, in particular, a controlled volume infusion pump may be useful.
For follow-on treatment, therapy may be continued with oral pentoxifylline alone.

Special Populations

Children
No experience is available concerning the use of Trental in children.

Hepatic impairment
A dose reduction - guided by individual tolerance - is necessary in patients with severely impaired liver function.

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

Other
Treatment must 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 stenoses of blood vessels supplying the brain); in such cases, the dose must only be increased gradually.

Administration
Usually, dosage is 400 mg pentoxifylline 2 to 3 times daily. Tablets are to be swallowed whole during or shortly after meal with sufficient amounts of liquid (approx. ½ glass).

CONTRAINDICATIONS
Trental must not be used

- in patients with hypersensitivity to pentoxifylline, other methylxanthines or any of the excipients of Trental.
- in patients with massive bleeding (risk of increased bleeding).
- in patients with extensive retinal bleeding (risk of increased bleeding).

PRECAUTIONS
At the first signs of an anaphylactic/anaphylactoid reaction, Trental must be discontinued, or the infusion be halted immediately, and a physician must be informed.
Particularly careful monitoring is required:

- in patients with severe cardiac arrhythmias.
- in patients with myocardial infarction.
- in hypotensive patients.
- in patients with impaired renal function (creatinine clearance below 30 ml/min).
- in patients with severely impaired liver function.
- in patients with increased bleeding (see “contraindications”)
- In patients treated concomitantly with pentoxyfylline and anti-vitamin K. or platelet aggregation inhibitors (See also section “ Interactions”).
- in patients treated concomitantly with pentoxifylline and antidiabetic agents. (See also section “ Interactions”.
- in patients treated concomitantly with pentoxifylline and ciprofloxacin (see also section “Interactions”)in patients treated concomitantly with pentoxifylline and theophylline (see also section “Interactions”).

INTERACTIONS

Precautions for use
The blood-sugar-lowering effect of insulin or oral antidiabetics may be potentiated. Therefore, 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.

Take into account
The blood-pressure-lowering effect of antihypertensive agents and other drugs with blood-pressure-lowering potential may be increased by Trental.

Concomitant administration of pentoxifylline and theophylline may increase theophylline levels in some patients. Therefore, there may be an increase in and intensification of adverse reactions from theophyllline.

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 I.

PREGNANCY
Insufficient experience has been gained concerning use in pregnancy. Therefore, it is recommended that Trental is not used during pregnancy.

LACTATION
Pentoxifylline passes into breast milk in minute quantities. Because insufficient experience has been gained, the physician must carefully weigh the possible risks and benefits before administering Trental in breast-feeding women.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS
Not applicable

INTERFERENCE WITH LABORATORY AND DIAGNOSTIC TESTS
Not applicable.

ADVERSE REACTIONS

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

System Organ Class	**Adverse Reaction**
Investigations	**Transaminases increased** (Transaminase elevation), **Blood pressure decreased** (Fall in blood pressure)
Cardiac disorders	**Arrhythmia** (Cardiac arrhythmia), **Tachycardia**, **Angina Pectoris**

Blood and lymphatic system disorders	**Thrombocytopenia** (Thrombopenia), **Leucopenia/neutropenia**
Nervous system disorders	**Dizziness, headache, meningitis aseptic** (Aseptic meningitis)
Gastrointestinal disorders	**Gastrointestinal disorder** (Gastrointestinal complaints), **Epigastric discomfort** (Gastric pressure), **Abdominal distension** (Fullness), **Nausea, Vomiting, Diarrhoea, Constipation, Hypersalivation**
Skin and subcutaneous tissue disorders	**Pruritus, Erythema** (Reddening of the skin), **Urticaria, Rash**
Vascular disorders	**Hot flush** (Flushes), **Haemorrhage** (Bleedings)
Immune system disorders	**Anaphylactic reaction, Anaphylactoid reaction, Angioedema** (Angioneurotic edema), **Bronchospasm, Anaphylactic shock (shock)**
Hepatobiliary disorders	**Cholestasis** (Intrahepatic cholestasis)
Psychiatric disorders	**Agitation, Sleep disorder** (Sleep disturbances)

OVERDOSE

Signs And Symptoms

Initial symptoms of acute overdose with pentoxifylline may be nausea, dizziness, tachycardia or a fall in blood pressure. Furthermore, signs such as fever, agitation, flush, loss of consciousness, areflexia, tonic-clonic convulsions and – as a sign of gastrointestinal bleeding – coffee-ground vomiting may occur.

Management

No specific antidote is known. If ingestion has only just taken place, attempts may be made to prevent further systemic absorption of the active ingredient by primary elimination of the toxin (e.g. gastric lavage) or by delaying its absorption (e.g. activated charcoal).

STORAGE

Store protected from light and moisture, at a temperature not exceeding 25°C

Pack Presentation: Blister pack 5 X 2 X 15'S

MANUFACTURED BY:
Zentiva Private Limited, Plot no. 3501-15, 6301 -13 & 16 meter road/c, G.I.D.C Estate, Ankleshwar-393002, Gujrat

MARKETED BY:
Sanofi India Limited, Sanofi House, CT Survey No 117-B, L & T Business Park, Saki Vihar Road, Powai, Mumbai- 400072

Source: CCDS Version 6 dated 15th April 2015 and CCDS ver 7 dated 29th May 2015
Updated: May 2018