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

DESCRIPTION

Active Ingredient

Pentoxifylline

Therapeutic or Pharmacological Class

Haemorheologic agent

Pharmaceutical Form(s)

Soultion for Intravenous administration

Composition

Each ampoule of 15 ml contains

Pentoxifylline B.P……..300mg

Water for Injection I.P… q.s

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

Dosage

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.

In case of the parenteral formulation, the infusion time must be at least 60 minutes per 100mg pentoxifylline.

- **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 1200mg 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 1200mg pentoxifylline be administered in a suitable carrier solution either as a continuous infusion over a period of 24 hours, or as an infusion of 600mg 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 Cases

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.

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

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.

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).

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

PRECAUTIONS
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 tendency due to e.g. anticoagulant medication or coagulation disorders. Concerning bleeding see contraindications
- 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 them).

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS
Not applicable

DRUG 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.

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 theophylline.

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.

ADVERSE REACTIONS
Particularly when Trental® is given in high doses or at high infusion rates the following reactions may occur: frequently, flushes, gastrointestinal complaints such as gastric pressure, fullness, nausea, vomiting or diarrhoea and, occasionally, cardiac arrhythmias (e.g. tachycardia).

Additionally, pruritus, reddening of the skin and urticaria may occasionally develop, as may, in isolated cases, severe anaphylactic / anaphylactoid reactions with e.g., angioneurotic oedema, bronchospasm, and sometimes even shock.

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.

Dizziness, headache, agitation and sleep disturbances may occasionally occur, as well as, in isolated cases, intrahepatic cholestasis and transaminase elevation, and aseptic meningitis.

Rarely, angina pectoris, fall in blood pressure, and – especially in patients with increased bleeding tendency – bleedings (e.g. on the skin and/or mucosae, in the stomach and/or intestine) may develop, as may – in isolated cases- thrombopenia.

OVERDOSE
- **Symptoms of overdose**

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.

- **Treatment of overdose**

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).

The treatment of acute overdose and the prevention of complications may necessitate general and specific intensive medical monitoring and therapeutic measures.

PREPARATION AND HANDLING

Physiological sodium chloride solution or for example Ringer's solution may be used as carriers for infusion. If other carrier solutions are selected, compatibility must be tested on an individual basis; only clear solutions must be infused.

Manufactured and Marketed by:
Aventis Pharma Limited

Registered Office:
54/A, Sir M.V.Road, Andheri (East) Mumbai – 400 093, Maharashtra India

Updated: December 2007
Source: CCDS Version 3, 24 April 2002.