SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Oxopurin 400

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged release caplet contains Pentoxifylline 400mg.

Excipient with known effect:

Each caplet contains approximately 105mg lactose.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Prolonged release caplet.

Pink, film-coated, caplet, scored on both sides.

The score line is not intended for breaking the caplet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the improvement of blood flow in the peripheral blood vessels.

4.2 Posology and method of administration

Chronic peripheral arterial occlusive disease at Fontaine stage IIb (intermittent claudication)
Unless otherwise prescribed, 1 Oxopurin 400mg prolonged-release caplet three times daily (equivalent to 1,200 mg pentoxifylline per day).

Special dosage instructions may be necessary for patients with low or fluctuating blood pressure levels.

In patients with impaired renal function (creatinine clearance less than 30 ml/min), the dose should be titrated to 50–70% of the standard dose, depending on individual tolerability, e.g. by taking 400 mg pentoxifylline twice daily instead of 400 mg pentoxifylline three times a day.

In the case of patients with severe hepatic dysfunction, a dose reduction is required, which should be decided by the doctor on an individual basis according to the severity of the illness and tolerability.

Inner ear dysfunction caused by circulatory disorders (including hardness of hearing, sudden hearing loss).
Unless otherwise prescribed, 1 Oxopurin 400mg prolonged-release caplet twice daily or three times a day (equivalent to 800–1,200 mg pentoxifylline per day).

In cases of severe circulatory disturbances, a combination with parenterally administered Pentoxifylline 100 mg or 300 mg ampoules (IV infusion) can accelerate the onset of action. The total daily dose (parenteral + oral) should essentially not exceed 1,200 mg pentoxifylline. Depending on the severity of symptoms, oral-only treatment, combined oral-parenteral treatment (IV infusion) or parenteral-only treatment (IV infusion) can be administered.

Elderly: No special dosage requirements.

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

Method and duration of administration

The prolonged-release caplets should be swallowed whole with plenty of liquid following a meal. Duration of use must be tailored to the individual clinical condition and is decided by the doctor.

The caplet must not be crushed, chewed or divided.

Note:

In the case of accelerated gastro-intestinal passage (laxatives, diarrhoea, surgical shortening of the intestine), elimination of caplet residues can occur in isolated cases. If premature elimination occurs only now and again, no importance need be attributed to the process.

4.3 Contraindications

Oxopurin 400 is contra-indicated in cases where there is known hypersensitivity to the active substance (pentoxifylline), other methyl xanthines 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, Oxopurin 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, Oxopurin 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 Oxopurin 400 to one or two caplets 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).

Oxopurin 400 contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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.

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

Oxopurin 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. Oxopurin 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 Oxopurin 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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

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

6.1 List of excipients

Lactose monohydrate, hypromellose, magnesium stearate, titanium dioxide (E171), macrogol 400, erythrosine aluminum lake (E127), indigo carmine aluminum lake (E132), quinoline yellow aluminum lake (E104), carnauba wax.

6.2 Incompatibilities

None known.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a dark place below 25°C.

6.5 Nature and contents of container

Blister.
Pack sizes: 50 or 100 caplets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

None.

7. MARKETING AUTHORISATION HOLDER

Dexcel Ltd., 1 Dexcel Street, Or Akiva 3060000, Israel

8. MARKETING AUTHORISATION NUMBER

011-41-23858-00

Revised in February 2021 according to MOH guidelines.