SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

ANTURAN® Tablets 200 mg
Sulfinpyrazone 200 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The active ingredient is 1,2-Diphenyl-3,5-dioxo-4-(2-phenylsulphinylethyl)-pyrazolidine (= 1sulfinpyrazone B.P.)
Each coated tablet contains 200 mg sulfinpyrazone.

3. PHARMACEUTICAL FORM

Coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Chronic, including tophaceous gout; recurrent gouty arthritis; hyperuricaemia.

4.2 Posology and Method of administration

ANTURAN is administered orally in tablet form with meals or milk.

Hyperuricaemia
Adults: 100-200mg daily increasing gradually (over the first two or three weeks) to 600mg daily (rarely 800mg), and maintained until the serum urate level has fallen within the normal range. Subsequent dosage should be reduced to the lowest level which maintains serum urate within the normal range. Maintenance dose may be as low as 200mg daily. Reduced dose required in renal impairment. Not to be used in severe renal impairment.

Children: Paediatric usage not established.
4.3 Contraindications

Acute attacks of gout. Treatment with anturan should not be initiated during an acute attack of gout.

Gastric and duodenal ulcer (overt or case-history).

Known hypersensitivity to sulfinpyrazone and other pyrazolone derivatives. Sulfinpyrazone is contra-indicated in patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or by other drugs with prostaglandin-synthetase inhibiting activity.

Severe parenchymal lesions of the liver or kidneys (also in the case history). Porphyria. Blood dyscrasias (also in the case history). Haemorrhagic diatheses (e.g. blood coagulation disorders).

In the treatment of chronic gout salicylates antagonise the action of ANTURAN and should not be given concurrently.

4.4 Special Warnings And Special Precautions For Use

During the early stages of treatment in patients with hyperuricaemia or gout, acute attacks of gout may be precipitated. To help prevent episodes of urolithiasis or renal colic, ensure adequate fluid intake and alkalinisation of the urine during initial stages of therapy.

Since ANTURAN may cause salt and water retention, caution is called for in patients with overt or latent heart failure.

For the early detection of a haematological abnormality, careful clinical supervision and full blood count should be done before and at regular intervals during treatment.

Use in caution in patients with impaired renal function.

In patients with an elevated plasma uric acid level and/or with a history of nephrolithiasis or renal colic, and also when resuming treatment after interruption of the medication, a cautious incremental dosage schedule should be adopted. As with any form of long-term uricosuric medication, renal function tests should be performed regularly, particularly in cases where there is pre-existing evidence of renal failure.

4.5 Interactions with other Medicaments and other forms of Interaction
Since ANTURAN may potentiate the action of coumarin-type anticoagulants, frequent estimation of prothrombin time should be undertaken when these drugs are given concurrently, and the dosage of anticoagulant adjusted accordingly.

ANTURAN may also potentiate the action of other plasma protein binding drugs such as hypoglycaemic agents and sulphonamides, which may necessitate a modification in dosage.

Penicillins (e.g. Penicillin G): inhibition of tubular secretion may raise plasma concentrations of penicillins.

Theophylline: activation of microsomal liver enzymes and resultant acceleration of metabolism lowers the plasma concentration of theophylline.

Phenytoin: displacement of phenytoin from its plasma protein-binding sites as well as inhibition of microsomal liver enzymes delays the metabolism of phenytoin, thus prolonging its half-life and raising its plasma concentration.

Substances affecting haemostasis: such substances, e.g. non-steroidal antirheumatic drugs, may exert a synergistic effect on the blood coagulation system and thus increase the risk of haemorrhage.

4.6 Pregnancy and Lactation

ANTURAN should be used with caution in pregnant women, weighing the potential risk against the possible benefits.

It is not known whether the active substance of anturan and/or its metabolite(s) pass into breast milk. For safety reasons mothers should refrain from taking the drug.

4.7 Effects on Ability to Drive and Use Machines

None stated.

4.8 Undesirable Effects

Gastro-intestinal tract:
Frequent: mild transient gastro-intestinal upsets, such as nausea, vomiting, diarrhoea.
In isolated cases: gastro-intestinal bleeding and ulcers.
Urogenital system:
Rare: acute renal failure (mostly reversible), especially with high initial dosages.
In isolated cases: salt and water retention.

Skin:
Rare: allergic skin reactions (e.g. drug rash, urticaria).

Blood:
In isolated cases: leucopenia, thrombocytopenia, agranulocytosis, aplastic anaemia.

Liver:
In isolated cases: hepatic dysfunction (increase in transaminases and phosphatase), jaundice and hepatitis.

4.9 Overdose

There is no antidote to anturan.

Signs and symptoms: nausea, vomiting, abdominal pains, diarrhoea, hypotension, cardiac arrhythmias, hyperventilation, respiratory disorders, impairment of consciousness, coma, epileptic seizures, oliguria or anuria, acute renal failure, renal colic.

Treatment: immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage preferably with mild alkaline solution such as sodium bicarbonate solution and supportive therapy as indicated.

Note that forced diuresis is of no value.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

ANTURAN lowers serum urate levels by blocking tubular reabsorption, thereby increasing renal excretion of uric acid. As a result of increased excretion, serum urate deposits are mobilised and tophi are no longer formed.

5.2 Pharmacokinetic Properties

After oral administration the active substance is absorbed rapidly and almost completely (>85%).
Following a single oral dose of 100mg or 200mg sulfinpyrazone, peak plasma concentrations of 5-6μg/ml or 13-22μg/ml, respectively, are attained after 1-2 hours. Sulfinpyrazone has a half-life of 2-4 hours.

Following repeated administration of sulfinpyrazone in a dosage of 400mg bid for 23 days, a significant decrease in the AUC values and an increase in the drug's clearance was observed as compared with the values recorded after a single dose. After multiple dosing with 400mg bid, the mean steady state concentration of sulfinpyrazone amounts to 5.1μg/ml, which corresponds to only half of the calculated value after a single dose (9.6μg.ml). The reason for this is an increase in total clearance brought about by the fact that the drug induces its own metabolism.

Sulfinpyrazone is metabolised by reduction to the sulphide and by oxidation to the sulphone and to hydroxy-compounds. The sulphide metabolite inhibits platelet aggregation in vitro about 12 times more strongly than sulfinpyrazone itself. In comparison with sulfinpyrazone the plasma concentrations of the sulphide metabolite are low. Peak sulphide concentrations are reached approx. 19 hours after administration of a single dose.

5.3 Preclinical Safety Data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, maize starch, aerosil 200, magnesium stearate, gelatin, sodium starch glycylate, sucrose, talc, povidone, titanium dioxide (E 171), polyethylene glycol, avicel, yellow iron oxide (E 172), red iron oxide (E172), black iron oxide (E172), ammonium hydroxide, shellac glaze, and propylene glycol (E490/E1520).

6.2 Incompatibilities

None stated.

6.3 Shelf Life

60 months
6.4 Special precautions for storage

Do not store above 25°C. Store in the original container in a dry place.

6.5 Nature and Contents of Container

Securitainers (polypropylene body with polyethylene cap) and child resistant/tamper evident loose fill packs of 84, blister packs of 84 and 112 and amber glass bottles of 100 tablets.

6.6 Instructions for Use/Handling

None stated.

7 MARKETING AUTHORISATION HOLDER

Amdipharm UK Limited
Regency House
Miles Gray Road
Basildon
Essex
SS14 3AF
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 20072/0025

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/03/2008

10 DATE OF REVISION OF THE TEXT