1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

PURBAC ADULT (tablet)

PURBAC DOUBLE STRENGTH (tablet)

PURBAC PAEDIATRIC SUSPENSION

COMPOSITION

PURBAC ADULT:

Each tablet contains 80 mg of trimethoprim and 400 mg of sulphamethoxazole.

Excipients:

Hydrogenated vegetable oil, magnesium stearate, microcrystalline cellulose, Nipastat, pregelatinised starch, sodium starch glycolate, starch maize

Preservative:

Nipastat 0,02 % *m/m*

Sugar free

PURBAC DOUBLE STRENGTH:

Each tablet contains 160 mg of trimethoprim and 800 mg of sulphamethoxazole.

Excipients:

Hydrogenated vegetable oil, magnesium stearate, microcrystalline cellulose, Nipastat, pregelatinised starch, sodium starch glycolate, starch maize

Preservatives:

Nipastat 0,02 % *m/m*

Sugar free

PURBAC PAEDIATRIC SUSPENSION:

Each 5 ml contains 40 mg of trimethoprim and 200 mg of sulphamethoxazole.

Excipients:

Aluminium magnesium silicate, aniseed oil, carmellose sodium, colour erythrosine powder (C.I. 45430), ethanol, Nipastat, polysorbate , purified water, sodium cyclamate, sucrose

Preservative:

Nipastat 0,3 % *m/v*

Contains sugar: Sucrose 3 g

Contains sweetener: Sodium cyclamate 20 mg

CATEGORY AND CLASS

A 20.2 Antimicrobial (chemotherapeutic) agents (other than antibiotics)

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Co-trimoxazole exerts its bactericidal action by the sequential blockade of two enzymes intervening in the biosynthesis of folinic acid in the micro-organism. Co-trimoxazole is bactericidal at concentrations at which the active ingredients, trimethoprim and sulphamethoxazole, are usually bacteriostatic. It is therefore often active against organisms resistant to one of the active ingredients thereby minimising the risk of bacterial resistance.

INDICATIONS

PURBAC is effective against a wide range of Gram-positive and Gram-negative organisms.

It is indicated for:

- Upper and lower respiratory tract infections e.g. acute and chronic bronchitis, bronchiectasis, tonsillitis, sinusitis and pharyngitis, otitis media, pneumonia and *Pneumocystis carinii* pneumonitis (see WARNINGS AND SPECIAL PRECAUTIONS).
- Renal and urinary tract infections e.g. pyelitis, pyelonephritis, urethritis, acute and chronic cystitis and cystopyelitis, including prostatitis.
- Gastrointestinal tract infections e.g. enteritis, typhoid and paratyphoid fever, typhoid carriage, bacillary dysentery and cholera (as an adjunct to fluid and electrolyte replacement).
- Genital tract infections - both male and female including gonococcal infections.
- Skin infections e.g. pyoderma, boils, furuncles, abscesses.
- Other bacterial infections - acute brucellosis, mycetoma except those caused by true fungi, nocardiosis, acute and chronic osteomyelitis.

CONTRAINDICATIONS

PURBAC is contraindicated in patients suffering from porphyria, liver parenchymal damage,

megaloblastic anaemia due to folic acid deficiency, severe renal insufficiency, and a history of hypersensitivity to sulphonamides or trimethoprim.

PURBAC should not be administered during pregnancy, to women prior to delivery, or to nursing mothers. It should also not be used in premature or newborn infants during the first few weeks of life.

WARNINGS AND SPECIAL PRECAUTIONS

A high incidence of side effects occurs in immunocompromised patients, such as those suffering from AIDS or patients receiving immunosuppressive therapy. The adverse effects include skin rash, recurrent fever, neutropenia, thrombocytopenia and raised liver enzyme values.

PURBAC may cause the occurrence of erythema multiforme, toxic dermal necrolysis and allergic vasculitis.

Treatment should be discontinued immediately when a rash appears because of the danger of severe allergic reactions.

PURBAC should be given with caution to patients with actual or possible folate deficiency because of possible interference with human folate metabolism by trimethoprim, and administration of folinic acid could be considered.

PURBAC should also be used with caution in patients receiving pyrimethamine as they may develop megaloblastic anaemia due to the trimethoprim component.

Adverse effects on the blood may be more severe in malnourished or elderly patients; therefore also appears to be an increased risk of thrombocytopenia in elderly patients concurrently receiving diuretics, mainly thiazides.

All patients receiving prolonged treatment with PURBAC should be given regular blood examinations.

PURBAC should be used cautiously and in reduced dosage in patients with impaired renal function. Because of the risk of crystalluria, an adequate fluid intake should be maintained and the administration of alkalis may be necessary if very large doses are used.

Excipients

PURBAC PAEDIATRIC SUSPENSION contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take PURBAC PAEDIATRIC SUSPENSION.

INTERACTIONS

Cross sensitivity has been observed between sulphamethoxazole and chemically related compounds such as some diuretics, particularly acetazolamide and thiazides, and the sulphonylurea hypoglycaemic medicines.

Sulphamethoxazole may potentiate the effects of some medicines, such as oral anticoagulants, methotrexate and phenytoin; this may be due to displacement of the

compound from plasma protein binding sites or to inhibition of metabolism.

High doses of sulphamethoxazole may have a hypoglycaemic effect; the antidiabetic effect of the sulphonylurea compounds may be enhanced by the concomitant administration of sulphamethoxazole.

The action of sulphamethoxazole may be antagonised by para-aminobenzoic acid and compounds derived from it, particularly the procaine group of local anaesthetics.

Paraldehyde has been reported to increase the acetylation of sulphamethoxazole with subsequent increased risk of crystalluria.

Sulphamethoxazole may interfere with some diagnostic tests including those for urea, creatinine and urinary glucose and urobilinogen.

Trimethoprim may potentiate the anticoagulant effect of warfarin. It also prolongs the half-life of phenytoin.

Trimethoprim has been reported to interact with a number of other medicines by interfering with their clearance; such medicines include digoxin, procainamide and tolbutamide.

Reversible deterioration in renal function has been reported in patients given trimethoprim and cyclosporine following renal transplantation.

Trimethoprim may interfere with some diagnostic tests including serum methotrexate assay where dihydrofolate reductase is used, and the Jaffe reaction for creatinine.

HUMAN REPRODUCTION

PURBAC should not be administered during pregnancy, to women prior to delivery, or to nursing mothers. It should also not be used in premature or newborn infants during the first few weeks of life (see CONTRAINDICATIONS).

DOSAGE AND DIRECTIONS FOR USE

Children 6 to 12 years:

One PURBAC ADULT tablet every 12 hours after meals.

Adults and children over 12 years:

The usual dose is two PURBAC ADULT tablets or one PURBAC DOUBLE STRENGTH tablet every 12 hours after meals. The maximum dose (for particularly severe cases) is three PURBAC ADULT tablets or one and a half PURBAC DOUBLE STRENGTH tablets every 12 hours. The minimum dosage for long-term treatment (longer than 14 days) is one PURBAC ADULT or a half PURBAC DOUBLE STRENGTH tablet every 12 hours.

Paediatric Dosage

PURBAC PAEDIATRIC SUSPENSION:

The following dosage structure is recommended: 6 mg trimethoprim plus 30 mg sulphamethoxazole per kg body mass daily which approximately corresponds to the following dosage according to age:

Children 6 to 12 years: Two medicine measures (10 ml) twice daily

(BOTTLE TO BE SHAKEN BEFORE USE).

In the treatment of acute infections, PURBAC should be administered for at least 5 days or at least 2 days after the symptoms have disappeared. If clinical improvement is not evident after 7 days therapy, the patients should be reassessed.

Dosage recommendation in renal impairment:

If PURBAC is indicated for patients with renal impairment, the following dosage scheme, based on creatinine clearance is suggested:

Creatinine clearance:

- Above 25 ml/min - standard dosage.
- 15 to 25 ml/min - standard dosage for a maximum of 3 days followed by half the standard daily dose.
- Below 15 ml/min - not to be administered unless haemodialysis facilities are available when half the standard daily dose may be given.

Measurements of plasma concentrations of sulphamethoxazole at intervals of 2 days are recommended in samples obtained 12 hours after administration of PURBAC.

If the concentration of total sulphamethoxazole exceeds 150 µg/ml then treatment should be interrupted until the value falls below 120 µg/ml.

No information is available for children with renal failure.

SIDE EFFECTS

Hypersensitivity reactions particularly involving the skin are among the most common adverse effects of PURBAC and are usually due to the sulphamethoxazole component. The Stevens-Johnson and Lyell's syndromes have been reported.

Adverse effects on the gastrointestinal tract may also occur fairly frequently.

Sulphamethoxazole:

Sulphamethoxazole may cause nausea, vomiting and diarrhoea.

Hypersensitivity reactions may occur. Those involving the skin include rashes, photosensitivity reactions, exfoliative dermatitis, toxic epidermal necrolysis (Lyell's syndrome) and erythema nodosum. A severe, potentially fatal form of erythema multiforme, associated with widespread lesions of the skin and mucous membranes, termed the Stevens-Johnson syndrome may occur. Systemic lupus erythematosus, particularly exacerbations of pre-existing disease, has also been reported.

Nephrotoxic reactions, which may result in renal failure, have been attributed to hypersensitivity to sulphamethoxazole.

Lumbar pain, haematuria, oliguria and anuria may occur due to crystallisation in the urine of sulphamethoxazole or its less soluble acetylated metabolite.

Blood disorders, mostly as a result of hypersensitivity reactions, may occur and include agranulocytosis, aplastic anaemia, thrombocytopenia, leucopenia, hypoprothrombinaemia and eosinophilia.

Acute haemolytic anaemia often associated with glucose-6-phosphate dehydrogenase deficiency may occur.

Other side effects which may be manifestations of a generalised hypersensitivity reaction to sulphamethoxazole include a syndrome resembling serum sickness, hepatotoxic reactions, myocarditis, pancreatitis, pulmonary eosinophilia and vasculitis including polyarteritis nodosa.

Anaphylaxis has been reported.

Sulphamethoxazole may cause cyanosis due to methaemoglobinaemia or sulphaemoglobinaemia.

Other side effects include effects of the eyes such as optic neuropathy or transient myopia, fever, hypothyroidism, and neurological reactions including ataxia, dizziness, fatigue, headache, insomnia, peripheral neuritis and vertigo.

Sulphamethoxazole may cause alterations of the bacterial flora in the gastrointestinal tract. There is, therefore, the possibility that pseudomembranous colitis may occur.

Slow acetylators of sulphamethoxazole may be at greater risk of adverse reactions than fast acetylators.

Trimethoprim:

Side effects caused by trimethoprim include pruritus, skin rash, fever, nausea, vomiting and sore mouth.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Possible symptoms of overdosage are those enumerated under side effects.

Treatment is symptomatic and supportive.

IDENTIFICATION

PURBAC ADULT: Flat white tablet with bevelled edges, engraved with Lennon logo on the one side and “PURBAC” on the other side.

PURBAC DOUBLE STRENGTH: White, oval, biconvex tablet, bisected on one side and debossed “C24” on the other side.

PURBAC PAEDIATRIC SUSPENSION: Pink, viscous suspension of pourable consistency with a characteristic aniseed odour.

PRESENTATION

PURBAC ADULT:

20 tablets are packed in a clear polyvinylchloride film sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton.

100 tablets are packed in a white polypropylene securitainer sealed with a white linear low-density polyethylene cap together with a white foam insert or violet rayon.

1 000 tablets are packed in an amber polyvinylchloride bottle sealed with a white high-density polyethylene pilfer proof cap with a white or red latex liner together with a white foam insert.

28 tablets are packed in a patient-ready metallised polyester lay-flat laminated with opaque

white linear low-density polyethylene sealed with a clear low-density polyethylene Ziploc. The lay-flat bags are packed in a clear low-density polyethylene bag.

PURBAC DOUBLE STRENGTH:

10 or 30 tablets are packed in a clear polyvinylchloride film sealed with an aluminium foil backing. One or more blister strips are packed into outer cardboard carton.

250 tablets are packed in an amber polyvinylchloride bottle sealed with a white high-density polyethylene cap with vertical ridges on the side together with a white foam insert.

28 tablets are packed in a patient-ready metallised polyester lay-flat laminated with opaque white linear low-density polyethylene sealed with a clear low-density polyethylene Ziploc. The lay-flat bags are packed in a clear low-density polyethylene bag.

PURBAC PAEDIATRIC SUSPENSION:

50 ml, 100 ml or 500 ml are packed into a brown high-density polyethylene bottle and sealed with a white low-density polyethylene snap cap. Each bottle is packed in an outer cardboard unit carton.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light and moisture.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

PURBAC ADULT:	J/20.2/339
PURBAC DOUBLE STRENGTH:	L/20.2/295
PURBAC PAEDIATRIC SUSPENSION:	K/20.2/241

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Dates of registration:

PURBAC ADULT:	16 May 1977
PURBAC DOUBLE STRENGTH:	30 January 1979
PURBAC PAEDIATRIC SUSPENSION:	07 December 1978

Date of the most recent amendment to the professional information as approved by the Authority: 30 January 1979

Botswana:	S2
PURBAC ADULT:	B9322715
PURBAC DOUBLE STRENGTH:	B9322720

Namibia:	NS2
PURBAC ADULT:	90/20.2/001146
PURBAC DOUBLE STRENGTH:	90/20.2/001147
PURBAC PAEDIATRIC SUSPENSION:	90/20.2/001149

ZA_PURBCOMB_7901_00