

150mm.

Directions for Use

Please Read Carefully!

LANOLONE TABLET

CONTENT

Each tablet contains Allopurinol 100 mg and Benzbromarone 20 mg.

DESCRIPTION

White round biconvex film-coated tablet embossed with "SPS", "L02" on one side, plain on the other side.

PHARMACODYNAMICS

Allopurinol is a xanthine-oxidase inhibitor. Allopurinol and its main metabolite oxipurinol lower the level of uric acid in plasma and urine by inhibition of xanthine oxidase, the enzyme catalysing the oxidation of hypoxanthine to xanthine and xanthine to uric acid.

Allopurinol also:

- reduces both the serum and urinary uric acid levels by inhibiting the formation of uric acid.
- decreases de novo purine synthesis via feedback inhibition of hypoxanthine-guanine phosphoribosyl-transferase.

Benzbromarone is a uricosuric drug which accelerates the excretion of uric acid towards normal by inhibiting tubular reabsorption of urate.

These two components of **Lanolone** complement each other in their action. As a result, the dose of each component can be kept at low level and their tolerance greatly increased. Even at a low dose daily, **Lanolone** reduces elevated serum uric acid levels. Existing deposits of uric acid are mobilized and excreted. Consequently, there is reduction in the frequency of attacks of acute gouty arthritis, reduction of urate load to be excreted via the kidney, prevention of acute uric acid nephropathy, improvement in joint mobility. In the long term, there is reduced risk of renal impairment caused by urate/uric acid, and dissolution of uric acid renal stones.

PHARMACOKINETICS

Allopurinol is active when given orally and is rapidly absorbed from the upper gastrointestinal tract. Estimated bioavailability vary from 67% to 90% with peak plasma levels generally occurring approximately 1.5 hours after oral administration, but fall rapidly and barely detectable after 6 hours.

Allopurinol is negligibly bound by plasma proteins and are likely to be concentrated mostly in the liver and intestinal mucosa. Approximately 20% of the ingested allopurinol is excreted in the faeces. Elimination of allopurinol is mainly by metabolic conversion to oxipurinol by xanthine oxidase and aldehyde oxidase, with less than 10% of the unchanged drug excreted in the urine. Allopurinol has a plasma half-life of about 1 to 2 hours.

Benzbromarone is partially absorbed from the gastrointestinal tract and is extensively bound to plasma proteins. It is metabolized in the liver, and is excreted mainly in the faeces with small amount being excreted in the urine.

INDICATION

- To reduce serum and urinary uric acid levels (primary and secondary hyperuricaemia).
- **Lanolone** is not suitable for use in acute attacks of gout.

RECOMMENDED DOSAGE

For oral administration.

One tablet daily after breakfast or lunch, or as prescribed by the physician.

CONTRAINDICATIONS

Lanolone is contraindicated in the following conditions:

- Severe hepatic and renal dysfunction.
- A tendency to form kidney stones (nephrolithic diathesis).
- Secondary hyperuricaemia resulting from blood disease or renal insufficiency.
- Hypersensitivity to allopurinol, benzbromarone or to any of the components of the formulation.
- During pregnancy and lactation.
- Acute attacks of gout.

WARNINGS AND PRECAUTIONS

Lanolone should be discontinued at the first appearance of skin rash or other signs which may indicate an allergic reaction. Hypersensitivity to allopurinol usually appears after some weeks of therapy, and more rarely immediately after beginning treatment. In some instances, a skin rash may be followed by more severe reactions such as exfoliative, urticarial and purpuric lesion as well as Stevens-Johnson syndrome, and/or generalized vasculitis, irreversible hepatotoxicity and even death.

Acute gout attack: **Lanolone** should not be started until an acute attack of gout has completely subsided, as further attacks may be precipitated. The initiation of treatment of **Lanolone** may precipitate an acute attack, and therefore a non-steroidal anti-inflammatory analgesic or colchicine should be used as a prophylactic and continued for at least one month after the hyperuricaemia has been corrected. For hyperuricaemia associated with cancer therapy, **Lanolone** treatment should be started before cancer therapy.

Hepatic or renal impairment: Allopurinol should be administered with care to patients with renal or hepatic impairments, and dosage may need to be reduced. Benzbromarone should not be used in people with known hepatic disease, and should be used with caution in people with a history of hepatic impairment or people who are also taking other medicines which may be potentially hepatotoxic. People who have an excess intake of alcohol are also likely to be more at risk of liver toxicity. Periodic liver function tests, renal function tests and complete blood cell counts should be performed in all patients on **Lanolone**.

Others: Increase fluid intake during **Lanolone** therapy to reduce the risk of xanthine and uric acid renal calculi. Additional alkalinisation of the urine may be considered.

Paediatric: There is little documented information since use is limited to children with enzyme disorders and to prevent uric acid nephropathy due to rapid breakdown of neoplastic cells.

Geriatric: Reduce the dose since there is a deterioration in renal and liver function of this group of patients.

Effects on ability to drive and use machines

Since side effects such as somnolence, vertigo and ataxia have been reported in patients receiving allopurinol, caution should be exercised before driving, using machinery or participating in activities where alertness is required.

DRUG INTERACTIONS

• **Azathioprine and 6-mercaptopurine:** Allopurinol reduces uric acid production by inhibiting the enzyme xanthine oxidase, which metabolises such potentially toxic drugs as mercaptopurine and azathioprine. Inhibition of xanthine oxidase can markedly prolong the effect of such drugs. The dose of mercaptopurine or azathioprine should be reduced to about 1/3 to 1/4 of the usual dose when allopurinol is given concurrently. Subsequent adjustment of doses of mercaptopurine or azathioprine should be made on the basis of therapeutic response and any toxic effects.

• **Salicylates and uricosuric agents:** Drugs with uricosuric activity (such as probenecid or large doses of salicylate) may accelerate the excretion of oxipurinol the active metabolite of allopurinol. This may decrease the therapeutic activity of allopurinol, but the significance should be assessed in each case.

• **Coumarin anticoagulants:** Patients may need careful monitoring, as there have been rare reports of increased effect of warfarin and other coumarin anticoagulants when co-administered with allopurinol.

• **Vidarabine (Adenine arabinoside):** Extra vigilance is necessary when vidarabine and allopurinol are used concomitantly as the plasma half-life of vidarabine may be increased resulting in enhanced toxic effects.

210mm.

TOKIWA A.P.THAILAND	Customer	เภสัชกรรมศรีประสิทธิ์	Size	150x210 mm	Confirm By
	Sales	ธำนิษฐ์	Color	1 COLOR	
	Artist	ยศ	Job Name	เอกสารกำกับ LANOLONE Malaysia (PIL0004) Rev:4	
	Date	01/02/63	Material		
	Modify		Machine		

หลังเซ็นต์ Confirm กรุณาส่ง E-mail : yot5864@hotmail.com หรือ แฟกซ์ 02-431-3158 กลับมาเพื่อยืนยันการผลิต

หน้า

150mm.

• **Chlorpropamide:** Caution is indicated as allopurinol may enhance the hypoglycaemic effect of chlorpropamide by competing for renal tubular secretion.

• **Phenytoin:** Allopurinol may inhibit hepatic oxidation of phenytoin, but the clinical significance has not been demonstrated.

• **Theophylline:** Inhibition of the metabolism of theophylline has been reported. The mechanism of the interaction may be explained by xanthine oxidase being involved in the biotransformation of theophylline in man. Theophylline levels should be monitored in patients starting or increasing allopurinol therapy.

• **Ampicillin / amoxicillin:** An increase in the frequency of skin rash has been reported among patients receiving ampicillin or amoxicillin concurrently with allopurinol compared with patients who are not receiving both drugs. The cause of the reported association has not been established. However, it is recommended that in patients receiving allopurinol an alternative to ampicillin or amoxicillin is used where available.

• **Cyclosporine:** Plasma concentration of cyclosporine may be increased during concomitant treatment with allopurinol. The possibility of enhanced cyclosporine toxicity should be considered if the drugs are co-administered.

• **Cytostatics:** With administration of allopurinol and cytostatics (e.g. cyclophosphamide, doxorubicin, bleomycin, procarbazine, alkyl halogenides), blood dyscrasias occur more frequently than when these active substances are administered alone. Blood count monitoring should therefore be performed at regular intervals.

• **Didanosine:** Plasma didanosine C_{max} and AUC values were approximately doubled with concomitant allopurinol treatment (300 mg daily) without affecting terminal half-life. Therefore, co-administration is generally not recommended. If concomitant use is unavoidable, a dose reduction of didanosine may be required, and patients should be closely monitored.

• **Thiazide diuretics:** Concomitant administration of allopurinol and thiazide diuretics may cause an increase in hypersensitivity reactions, particularly in patients with impaired renal function.

• **Angiotensin-converting-enzyme (ACE) inhibitors:** An increased risk of hypersensitivity has been reported when allopurinol is given with ACE inhibitors especially in renal impairment.

• **Aluminium hydroxide:** If aluminium hydroxide is taken concomitantly, allopurinol may have an attenuated effect. There should be an interval of at least 3 hours between taking both medicines.

PREGNANCY AND LACTATION

There is inadequate evidence of safety of **Lanolone** in human pregnancy. This drug should only be used during pregnancy if clearly needed.

Allopurinol is excreted in human breast milk. However, the effect of allopurinol on the nursing infant is unknown. Caution should be exercised when allopurinol is administered to a nursing woman.

SIDE EFFECTS

Infections and infestations

Very rare: Furuncle

Blood and lymphatic system disorders

Very rare: Agranulocytosis, aplastic anaemia, thrombocytopenia

Immune system disorders

Uncommon: Hypersensitivity

Very rare: Angioimmunoblastic T-cell lymphoma, anaphylactic reaction

Metabolism and nutrition disorders

Very rare: Diabetes mellitus, hyperlipidaemia

Psychiatric disorders

Very rare: Depression

Nervous system disorders

Very rare: Coma, paralysis, ataxia, neuropathy peripheral, paraesthesia, somnolence, headache, dysgeusia

Eye disorders

Very rare: Cataract, visual impairment, maculopathy

Ear and labyrinth disorders

Very rare: Vertigo

Cardiac disorders

Very rare: Angina pectoris, bradycardia

Vascular disorders

Very rare: Hypertension

Gastrointestinal disorders

Uncommon: Vomiting, nausea

Very rare: Haematemesis, steatorrhoea, stomatitis, change of bowel habit

Hepatobiliary disorders

Uncommon: Abnormal liver function test

Rare: Hepatitis (including hepatic necrosis and granulomatous hepatitis)

Skin and subcutaneous tissue disorders

Common: Rash

Rare: Stevens-Johnson syndrome/toxic, epidermal necrolysis

Very rare: Angioedema, drug eruption, alopecia, hair colour changes

Renal and urinary disorders

Very rare: Haematuria, azotaemia

Reproductive system and breast disorders

Very rare: Male infertility, erectile dysfunction, gynecomastia

General disorders and administration site conditions

Very rare: Oedema, malaise, asthenia, fever

Investigations

Common: Blood thyroid stimulating hormone increased

SYMPTOMS AND TREATMENT OF OVERDOSE

Symptoms: Most likely reactions would be gastrointestinal intolerance. Massive absorption may lead to a considerable inhibition of xanthine oxidase, which should have no untoward effects unless 6-mercaptopurine and/or azathioprine is taken concomitantly.

Treatment: There is no specific antidote for overdose. Maintain adequate hydration to ensure maximum diuresis, which facilitates the excretion of allopurinol and its metabolites. Allopurinol is dialyzable. However, the usefulness of haemodialysis or peritoneal dialysis in the management of allopurinol overdose is unknown. Therefore, dialysis may be resorted to if considered necessary.

PACKING / PACK SIZES

Blister strip of 10 tablets. Box of 100, 200 and 500 tablets.

STORAGE CONDITIONS AND PHARMACEUTICAL PRECAUTIONS

Store in a cool dry place, below 30°C.

Protect from light.

Keep out of reach of children.

Jauh! daripada kanak-kanak.

SHELF-LIFE: Please refer to the outer box label.

MANUFACTURED BY

SRI PRASIT PHARMA CO., LTD.
216 Moo 6, Suanluang, Krathum Baen,
Samut Sakhon 74110, Thailand.

DATE OF REVISION: June 2019

PIL0004 Rev:4

210mm.

TOKIWA A.P. (THAILAND)	Customer	เภสัชกรรมศรีประสิทธิ์	Size	150x210 mm	Confirm By
	Sales	ธำนิษฐ์	Color	1 COLOR	
	Artist	ยศ	Job Name	เอกสารกำกับ LANOLONE Malaysia (PIL0004)Rev:4	
	Date	04/02/63	Material		
	Modify		Machine		

หลังจากนี้ Confirm กรุณาส่ง E-mail : yot5864@hotmail.com หรือ แฟกซ์ 02-431-3158 กลับมาเพื่อยืนยันการผลิต

หลัง