PROFESSIONAL INFORMATION

LANCAP OTC

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

LANCAP OTC 15 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains lansoprazole 15 mg

Each capsule contains sugar (sucrose 16,55 mg, sugar spheres 70,0 mg).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Gastroresistant capsule, hard.

LANCAP OTC capsules are white/red-brownish (body: white, cap: red-brownish) capsules filled with a white to light brown or slightly pink coloured pellets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LANCAP OTC is indicated in adults for the temporary short-term relief of heartburn and hyperacidity.

4.2 Posology and method of administration

Posology

LANCAP OTC should preferably be taken before a meal.

The maximum daily dose is 15 mg once daily for a maximum of 14 days.

Special populations

Elderly:

No dose adjustment is necessary. However, 15 mg per day is the maximum daily dose.

Renal impairment:

No dose adjustment is necessary in renal failure - this also applies to patients on dialysis.

Paediatric population

LANCAP OTC is not indicated for use in children as clinical data is limited.

Method of administration

LANCAP OTC should be taken at least 30 minutes before a meal (see section 5.2). Capsules should be swallowed whole with liquid.

For patients with difficulty swallowing; the capsules may be emptied, but the contents may not be chewed or ground.

Missed dose:

Medical practitioners should advise patients who forget to take LANCAP OTC to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- hypersensitivity to lansoprazole or to any of the ingredients of LANCAP OTC
- pregnancy and lactation
- severe hepatic impairment
- LANCAP OTC is contraindicated with atazanavir or nelfinavir, as it substantially reduces exposure to thehuman immunodeficiency virus (HIV) protease inhibitor (see section 4.4).

4.4 Special warnings and precautions for use

Safety and efficacy in children:

Safety and efficacy in children have not been established.

Diagnosis of reflux oesophagitis:

Diagnosis of reflux oesophagitis should be confirmed by endoscopy.

Exclusion of malignant ulcers:

Treatment with LANCAP OTC may alleviate the symptoms of malignant ulcers and can delay diagnosis. Therefore, in the presence of symptoms such as, significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, or melaena, and when gastric ulcer is suspected or present, the possibility of malignancy of gastric ulcer or a malignant disease of the oesophagus should be excluded prior to treatment with LANCAP OTC.

Occurrence of acute interstitial nephritis:

Acute interstitial nephritis has been observed in patients taking proton pump inhibitors (PPIs), including LANCAP OTC. Acute interstitial nephritis may occur at any point during therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue LANCAP OTC if acute interstitial nephritis develops (see section 4.3).

Malabsorption:

Daily treatment with acid-suppressing medicines such as LANCAP OTC over a long period of time (e.g. longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. Cyanocobalamin deficiency occurring with acid-suppressing therapy has been reported. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.

Proton pump inhibitors such as LANCAP OTC have also been reported to impair the bioavailability of dietary vitamin C. Fat malabsorption (secondary to increased deconjugation of bile acids caused by bacterial overgrowth in the jejunum) was reported when patients were treated with proton pump inhibitors such as LANCAP OTC. Proton pump inhibitors such as LANCAP OTC can cause calcium malabsorption (see Bone fracture).

Subacute cutaneous lupus erythematosus (SCLE):

Proton pump inhibitors such as LANCAP OTC are associated with cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping LANCAP OTC. SCLE after previous treatment with a proton pump inhibitor such as LANCAP OTC may increase the risk of SCLE with other proton pump inhibitors.

Increased risk of Clostridium difficile associated diarrhoea:

LANCAP OTC may be associated with an increased risk of *Clostridium difficile* associated diarrhoea (CDAD). A diagnosis of CDAD should be considered for patients taking LANCAP OTC who develop diarrhoea that does not stop. Symptoms include watery stool, abdominal pain, and fever, and patients may go on to develop more serious intestinal conditions. Factors that may predispose an individual to developing CDAD include advanced age, certain chronic medical conditions, and taking broad spectrum antibiotics. Treatment for CDAD includes the replacement of fluids and electrolytes and the use of special antibiotics. Patients should use the lowest dose and shortest duration of LANCAP OTC therapy appropriate to the condition being treated.

Bone fracture:

LANCAP OTC therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term therapy (a year or longer) mainly in the elderly or in the presence of other recognised risk factors. Patients should use the lowest dose and shortest duration of LANCAP OTC therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines and should receive appropriate care (see section 4.8).

Occurrence of hypomagnesaemia, hypocalcaemia and hypokalaemia:

Severe hypomagnesaemia has been reported in patients treated with LANCAP OTC for at least 3

months to one year. Hypomagnesaemiaalso produces impaired parathyroid hormone secretion which may lead to hypocalcaemia. Most patients had concomitant hypercalcaemia and normal parathyroid hormone levels; therefore it confirms hypomagnesaemia as the primary deficit. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular dysrhythmia can occur, but may begin slowly and be overlooked. In most patients affected, symptoms improved after magnesium replacement and discontinuation of LANCAP OTC.

For patients expected to be on prolonged treatment or who take LANCAP OTC with digoxin or medicines which may cause hypomagnesaemia (e.g. diuretics), healthcare professionals should consider measuring magnesium levels before starting and during treatment with LANCAP OTC (see section 4.8).

Lansoprazole decreases gastric acid secretion by targeting hydrogen (H)+, potassium (K)+- adenosine triphosphatase (ATPase) in acidic conditions, hypokalaemia is not generally introduced by LANCAP OTC alone, but in extreme alkalosis or an impaired K+ -recycling system, LANCAP OTC may cause hypokalaemia unrelated to hypomagnesaemia

Concomitant use with methotrexate:

Concomitant use of LANCAP OTC with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of LANCAP OTC may be considered in some patients (see section 4.5).

Effects related to acid inhibition:

During long-term treatment, gastric glandular cysts have been reported in increased frequency. These physiological changes result from pronounced inhibition of gastric acid secretion.

Gastrointestinal infections caused by bacteria:

Decreased gastric acidity increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with LANCAP OTC may lead to an increased risk of gastro-intestinal infections such

as *Salmonella*, and *Campylobacter, Shigella or Clostridium difficile*.

Helicobacter pylori (H. pylori):

In patients suffering from gastroduodenal ulcers, the possibility of *H. pylori* infection as an etiological factor should be considered.

Effect on central nervous system:

LANCAP OTC may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.

Possible porphyrinogenicity:

Lansoprazole, as in LANCAP OTC, is possibly porphyrinogenic and should be used only when no safer alternative is available, and precautions should be considered in all patients.

Long term use:

Because of limited safety data for patients on maintenance treatment for longer than 1year, regular review of the treatment should be performed in these patients.

Colitis:

Colitis has occurred in patients taking lansoprazole as contained in LANCAP OTC. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.

Interference with laboratory tests:

Increased Chromogranin A (CgA) levels may interfere with investigations for neuroendocrine tumours. To avoid this interference, LANCAP OTC treatment should be stopped for at least 5 days before CgA measurements (see section 5.1). If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

Information on excipients of LANCAP OTC:

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

LANCAP OTC contains less than 1 mmol (0,023g) per capsule, that is to say essentially 'sodium free'.

Paediatirc population (bold)

Safety and efficacy in children has not yet been established

4.5 Interaction with other medicines and other forms of interaction

Effects of LANCAP OTC on other medicines

Medicines with pH dependent absorption:

LANCAP OTC may interfere with the absorption of medicines where gastric pH is critical to bioavailability (e.g. ampicillin esters, iron salts).

HIV Medicines:

It has been shown that co-administration of atazanavir with protonpump inhibitors such as LANCAP OTC results in a substantial reduction in the bioavailability of atazanavir. Therefore, LANCAP OTC must not be co-administered with atazanavir and nelfinavir (see section 4.3).

Ketoconazole and itraconazole:

The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole, as in LANCAP OTC, may result in subtherapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Digoxin:

Co-administration of LANCAP OTC and digoxin may lead to increased digoxin plasma levels. The

plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending LANCAP OTC treatment.

Medicines metabolised by cytochrome P450 (CYP450) enzymes:

LANCAP OTC may increase plasma concentrations of medicines that are metabolised by cytochrome P3A4 (CYP3A4). Caution is advised when combining LANCAP OTC with medicines which are metabolised by this enzyme and have a narrow therapeutic window.

Theophylline:

LANCAP OTC reduces the plasma concentration of theophylline potentially decreasing the expected clinical effect at the required dose.

Patients may require additional titration of the theophylline dosage when treatment with LANCAP OTC is commenced or discontinued, to ensure clinically effective blood levels. Caution is thus advised when used in combination.

Tacrolimus:

Co-administration of LANCAP OTC may cause an increase in tacrolimus (a CYP3A and P-gp substrate) plasma concentrations and result in a decreased clearance. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with LANCAP OTC is initiated or ended.

Medicines transported by P-glycoprotein:

Lansoprazole, as in LANCAP OTC, has been observed to inhibit the transport protein, P-glycoprotein (P-gp) *in vitro*. The clinical relevance of this is unknown.

Effects of other medicines on LANCAP OTC

Medicines which inhibit CYP2C19

Fluvoxamine:

Fluvoxamine may increase the plasma concentration of lansoprazole therefore a dose reduction may

need to be considered in patients taking these medicines concomitantly.

Medicines which induce CYP2C19 and CYP3A4:

Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John's wort (*Hypericum perforatum*) can reduce the plasma concentrations of lansoprazole in LANCAP OTC.

Others

Warfarin:

There have been reports of increased international normalised ratio (INR) and prothrombin time in patients receiving PPIs such as LANCAP OTC and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with LANCAP OTC and warfarin concomitantly may need to be monitored for increase in INR and prothrombin time, especially when initiating or ending concomitant treatment.

Sucralfate/Antacids:

The bioavailability and absorption of LANCAP OTC may be decreased with concomitant administration of sucralfate/antacids. LANCAP OTC should be taken at least 1 hour after taking these medications.

Nonsteroidal anti-inflammatory medicines:

No clinically significant interactions of LANCAP OTC with nonsteroidal anti-inflammatory medicines have been demonstrated, although no formal interactions studies have been performed.

Methotrexate:

Although lansoprazole as contained in LANCAP OTC has been reported not to affect the pharmacokinetics of methotrexate, concomitant use with high-dose methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. Therefore, in settings where high-dose methotrexate is used a temporary withdrawal of LANCAP OTC may need to be considered.

4.6 Fertility, pregnancy and lactation

Pregnancy

LANCAP OTC is contraindicated in pregnancy and lactation (see section 4.3). Safety in pregnancy and lactation has not been established.

Adequate and well-controlled studies in humans have not been done.

Breastfeeding

It is not known whether lansoprazole, as contained in LANCAP OTC, is distributed into breast milk. However, lansoprazole or its metabolites are known to be distributed into the milk of rats. Lansoprazole has been shown to cause tumourigenic effects in animals and is therefore not recommended during breastfeeding (see section 4.3).

4.7 Effects on ability to drive and use machines

Adverse reactions such as dizziness, vertigo, visual disturbances and somnolence may occur when taking LANCAP OTC. Under these conditions the ability to react may be decreased. Patients should therefore be advised not to drive or operate machinery until they know how LANCAP OTC affects them.

4.8 Undesirable effects

a. Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Side effects**
Infections and Infestations	Less frequent	Candidiasis, flu syndrome, infection
Neoplasms benign and malignant (including cysts and polyps)	Less frequent	Carcinoma, laryngeal neoplasia, skin carcinoma, gastric nodules, fundic polyps

Blood and lymphatic system disorders	Less frequent	Thrombocytopaenia, anaemia, leukopaenia, neutropenia, eosinophilia, agranulocytosis, pancytopenia, haemolysis, lymphadenopathy
Immune system disorders	Less frequent	Allergic reaction, bronchospasm, angioedema, anaphylaxis, anaphylactic shock, acute interstitial nephritis
Endocrine disorders	Less frequent	Diabetes mellitus, goitre, hypothyroidism
Metabolism and nutrition disorders	Less frequent Frequency unknown	Avitaminosis, dehydration, gout, hyperglycaemia/hypoglycaemia, peripheral oedema, weight gain/loss, anorexia Hypomagnesaemia: severe hypomagnesaemia can correlate with hypocalcaemia and may result in hypokalaemia

Psychiatric disorders	Less frequent	Abnormal dreams, agitation, amnesia, anxiety, apathy, confusion, depersonalisation, depression, emotional lability, hallucinations, hostility aggravated, libido decreased/increased, nervousness, sleep disorder, dementia, neurosis, insomnia
Nervous system disorders	Frequent Less frequent	Headache, dizziness Convulsion, diplopia, hemiplegia, hypoesthesia, hyperkinesia, hypertonia, paraesthesia, restlessness, thinking abnormality, somnolence, parosmia, tremor, vertigo
Eye disorders	Less frequent	Abnormal vision, amblyopia, blepharitis, blurred vision, cataract, conjunctivitis, dry eyes, eye pain, photophobia, retinal degeneration, visual field defect, visual disturbances
Ear and labyrinth disorders	Less frequent	Deafness, ear disorder, otitis media, tinnitus

Cardiac disorders	Less frequent	Angina, dysrhythmia, bradycardia, myocardial infarction, palpitations, shock (circulatory failure), tachycardia, cardiospasm
Vascular disorders	Less frequent	Vasodilation, cerebrovascular accident/cerebral infarction, hypertension/hypotension, migraine, syncope
Respiratory, thoracic and mediastinal disorders	Less frequent	Asthma, bronchitis, cough increased, dyspnoea, epistaxis, haemoptysis, hiccough, laryngeal neoplasia, pharyngitis, pleural disorder, pneumonia, respiratory disorder, upper respiratory inflammation/infection, rhinitis, sinusitis, stridor, parosmia

Gastrointestinal disorders	Frequent	Diarrhoea, dry mouth or throat, nausea, vomiting, constipation, abdominal pain, flatulence
	Less frequent	Abnormal stools, anorexia, bezoar, cholelithiasis, colitis, dyspepsia, dysphagia, enteritis, eructation, faecal discolouration, gastric nodules/fundic gland polyps, gastritis, gastroenteritis, gastrointestinal anomaly, abdomen enlarged, gastrointestinal disorder, gastrointestinal haemorrhage, glossitis, gum haemorrhage, haematemesis, increased appetite, increased salivation, melena, mouth ulceration, oesophageal candidiasis, oesophageal stenosis, oesophageal ulcer, oesophagitis, oral moniliasis, rectal disorder, rectal haemorrhage, stomatitis, taste abnormalities, tenesmus, thirst, tongue disorder, ulcerative colitis, ulcerative stomatitis, pancreatitis (sometimes fatal)
	Frequency unknown	Collagenous colitis, gastric glandular cysts

Hepatobiliary disorders	Frequent Less frequent	Elevation in hepatic enzymes Hepatitis, jaundice, liver injury, hyperbilirubinaemia, cholelithiasis
Skin and subcutaneous tissue disorders	Frequent Less frequent	Skin rash, pruritus, urticaria Acne, alopecia, contact dermatitis, dry skin, erythema multiforme, fixed eruption, nail disorder, skin disorder, sweating, Stevens-Johnson syndrome or toxic-epidermal necrolysis, photosensitivity, petechiae, purpura, hair disorder, maculopapular rash
Musculoskeletal, connective tissue and bone disorders	Less frequent	Asthenia, arthralgia, arthritis, back pain, myalgia, fracture of the hip, wrist or spine, joint disorder, leg cramps, musculoskeletal pain, myasthenia, neck pain, neck rigidity, pelvic pain, ptosis, synovitis, bone disorder
Renal and urinary disorders	Less frequent	Dysuria, interstitial nephritis, kidney calculus, kidney pain, polyuria, urethral pain, urinary frequency, urinary tract infection, urinary urgency, urination impaired, urinary retention

Reproductive system and breast disorders	Less frequent	Abnormal menses, breast enlargement, breast pain, breast tenderness, dysmenorrhoea, gynaecomastia, impotence, leucorrhoea, menorrhagia, menstrual disorder, penis disorder, vaginitis, testes disorder, galactorrhoea
General disorders and administrative site conditions	Frequent Less frequent	Fatigue Asthenia, chest pain, chills, fever, halitosis, malaise, oedema, pain
Investigations	Less frequent	Hyponatraemia, increase in cholesterol and triglyceride levels

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website. An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 OVERDOSE

Signs and symptoms:

The effects of overdose on lansoprazole as in LANCAP OTC, in humans are not known (although the acute toxicity is likely to be low). However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.

Refer to section 4.8. for possible symptoms of lansoprazole overdose.

Management of overdose:

Treatment is symptomatic and supportive. In the case of suspected overdose, the patient should be monitored. Lansoprazole, as contained in LANCAP OTC, is not significantly eliminated by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors.

ATC code: A02BC03.

Pharmacological classification: A. 11.4.3 Medicines acting on the gastrointestinal tract.

Mechanism of action

Lansoprazole is an inhibitor of the gastric H+ K+-ATPase (proton pump). Lansoprazole inhibits gastric acid secretion in a dose related manner irrespective of the source of stimulation. Gastric secretory functions recover gradually following discontinuation of the medicine. Lansoprazole has no effect on histamine, gastrin or cholinergic receptors.

5.2 Pharmacokinetic properties

Absorption:

Following oral administration, lansoprazole is well absorbed with a resultant bioavailability of approximately 78 %. The bioavailability is decreased if lansoprazole is taken with food. Peak serum concentrations are achieved approximately 1 - 2 hours following ingestion.

Distribution:

Lansoprazole is highly protein bound (97 %).

Biotransformation:

Lansoprazole is extensively metabolised via the hepatic cytochrome P450 system to the inactive,

sulphated metabolites – sulphone, sulphide and 5-hydroxyl-lansoprazole. The half-life for lansoprazole is 1,4 - 1,5 hours.

Elimination:

The main route of elimination is via the bile with 15 - 30 % of lansoprazole been excreted via the kidneys as the hydroxylated metabolite.

Pharmacokinetics in special patient groups

Elderly:

The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50 - 100 %. Because the mean half-life in the elderly remains between 1,9 - 2,9 hours, repeated once daily dosing does not result in accumulation of lansoprazole. Peak plasma levels are not increased in the elderly therefore no dose adjustment is necessary.

Renal impairment:

In patients with severe renal insufficiency, plasma protein binding decreases by 1,0 - 1,5 % after administration of 60 mg of lansoprazole. Patients with renal insufficiency have a shortened elimination half-life and decreased total AUC (free and bound). AUC for free lansoprazole in plasma, however, is not related to the degree of renal impairment, and C_{max} and T_{max} are not different from patients with healthy kidneys. No dosage adjustment is necessary in patients with renal impairment.

Hepatic impairment:

In patients with various degrees of chronic hepatic disease, the mean plasma half-life of lansoprazole is prolonged from 1,5 hours to 3,2 hours to 7,2 hours. An increase in mean area under the plasma drug concentration-time curve (AUC) of up to 500 % has been observed at steady state in hepatically-impaired patients compared to healthy patients. Dose reduction in patients with severe hepatic disease should therefore be considered.

Race:

The mean AUC of lansoprazole in Asian patients is approximately twice that observed in whites or African Americans, since the former population are more likely to have the CYP2C19 genotype that correlates with slow metabolism of proton pump inhibitors. This finding may contribute to heightened efficacy and/or toxicity in the Asian population.

CYP2C19 poor metabolisers:

CYP2C19 is subject to genetic polymorphism and 2 - 6 % of the population, called poor metabolisers (PMs), are homozygote for a mutant CYP2C19 allele and therefore lacks a functional CYP2C19 enzyme. The exposure of lansoprazole is up to 5-fold higher in PMs than in extensive metabolisers (EMs).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium hydrogen phosphate dehydrate

Gelatine capsules

Maize starch

Methacrylic acid – ethyl acrylate copolymer (1:1) 30 % dispersion

Polysorbate 80

Polyvinylpyrrolidone

Sodium lauryl sulphate

Sucrose

Sugar spheres

Talc

Titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a dry place at or below 25 ºC.

Keep the capsules in the original container until required for use.

6.5 Nature and contents of container

LANCAP OTC 15 mg capsules are available in white HDPE bottles closed with a polypropylene tamper-evident cap with mounted desiccant insert containing 14 capsules.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER(S)

A49/11.4.3/0229

9. DATE OF FIRST AUTHORISATION

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07 August 2024