APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

LANCAP 15 mg capsules

LANCAP 30 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

LANCAP 15 mg: Each capsule contains 15 mg lansoprazole.

LANCAP 30 mg: Each capsule contains 30 mg lansoprazole.

LANCAP contains sugar (sucrose) in the following quantities:

LANCAP 15 mg (16,55 mg and sugar spheres 70,0 mg)

LANCAP 30 mg (33,10 mg and sugar spheres 140,0 mg)

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsules.

LANCAP 15 mg: Capsules filled with white to light brown or slightly pink coloured pellets.

The body of the hard gelatine capsule is white and the cap is red-brownish coloured.

LANCAP 30 mg: Capsules filled with white to light brown or slightly pink coloured pellets.

The body and cap of the hard gelatine capsule are white.

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4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- LANCAP 30 mg is indicated for the short-term treatment of gastric and duodenal ulcers and reflux oesophagitis.
- LANCAP is indicated for *Helicobacter pylori*-positive duodenal ulcers in conjunction with appropriate antibiotics as part of an eradication programme.

4.2 Posology and method of administration

Posology

Gastric ulcer:

30 mg once a day for up to eight weeks.

Duodenal ulcer:

30 mg once a day for up to four weeks.

LANCAP is indicated for *Helicobacter pylori* positive ulcers, as part of an eradication program with appropriate antibiotics.

Oesophagitis due to gastro-oesophageal reflux:

30 mg once a day for four weeks. Depending on the endoscopic results, a repeat course of 4 weeks may be necessary.

Maintenance treatment for the prevention of gastro-oesophageal reflux:

15 mg once a day for a maximum period of one year.

Functional dyspepsia:

Adults: 15 – 30 mg once a day for 2 to 4 weeks.

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Special populations

Elderly: No dose adjustment is necessary. However, 30 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.

Method of administration

LANCAP should preferably be taken before a meal.

Missed dose:

Doctors should advise patients who forget to take LANCAP 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.
- Pregnancy and lactation (see section 4.6).
- Severe liver impairment.
- LANCAP is contraindicated with atazanavir or nelfinavir, as it substantially reduces exposure to the HIV-protease inhibitor (see section 4.5).

4.4 Special warnings and precautions for use

Diagnosis of reflux oesophagitis:

Diagnosis of reflux oesophagitis should be confirmed by endoscopy.

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Exclusion of malignant ulcers:

Treatment with LANCAP 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.

Effect of prolonged use:

Daily treatment with acid-suppressing medicines such as LANCAP over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B_{12}) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.

Proton pump inhibitors such as LANCAP 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, has also been reported with proton pump inhibitors such as LANCAP treatment. For the suggestion that proton pump inhibitors such as LANCAP can cause calcium malabsorption, (see section 4.8).

Subacute cutaneous lupus erythematosus (SCLE):

Proton pump inhibitors such as LANCAP are associated with very infrequent 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

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should consider stopping LANCAP. SCLE after previous treatment with a proton pump inhibitor such as LANCAP may increase the risk of SCLE with other proton pump inhibitors.

Increased risk of *Clostridium difficile* associated diarrhoea:

LANCAP may be associated with an increased risk of *Clostridium difficile* associated diarrhoea (CDAD). A diagnosis of CDAD should be considered for patients taking LANCAP who develop diarrhoea that does not stop. Patients should use the lowest dose and shortest duration of LANCAP therapy appropriate to the condition being treated.

Bone fracture:

LANCAP 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 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:

Severe hypomagnesaemia has been reported in patients treated with LANCAP for at least 3 months to one year. Hypomagnesemia also produces impaired parathyroid hormone secretion which may lead to hypocalcemia. 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. For patients expected to be on prolonged treatment or who take LANCAP with digoxin or medicines which may cause hypomagnesaemia (e.g. diuretics), health care professionals should consider measuring magnesium levels before starting and during treatment with LANCAP (see section 4.8).

Concomitant use with methotrexate:

Concomitant use of LANCAP 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 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.

Decreased gastric acidity increases gastric counts of bacteria normally present in the gastro-intestinal tract. Treatment with LANCAP may lead to an increased risk of gastro-intestinal infections such as *Salmonella*, and *Campylobacter*, *Shigella* or *Clostridium difficile*.

Helicobacter pylori:

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

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Effect on central nervous system:

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

Acute Interstitial Nephritis:

Acute interstitial nephritis has been observed in patients taking proton pump inhibitors (PPIs) including LANCAP. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction and is associated with damage to the tubulointerstitium, leading to acute kidney injury. Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non- specific symptoms of decreased renal function (e.g., malaise, nausea, anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extra-renal manifestations (e.g., fever, rash or arthralgia). Interstitial nephritis may lead to renal failure. Discontinue LANCAP if acute interstitial nephritis develops (see section 4.8).

Long term use:

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

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Colitis:

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

Interference with laboratory tests:

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, LANCAP 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:

LANCAP 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 mal-absorption or sucrase-isomaltase insufficiency should not take LANCAP.

Paediatric population

Safety and efficacy in children:

Safety and efficacy in children has not been established.

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4.5 Interaction with other medicines and other forms of interaction

Effects of LANCAP on other medicines

Medicines with pH dependant absorption

LANCAP causes a profound and long-lasting inhibition of gastric acid secretion, therefore it is possible that LANCAP may interfere with the absorption of medicines where gastric pH is an important determinant of bioavailability (e.g. itraconazole, ketoconazole, posaconazole, ampicillin esters, iron salts, digoxin, atazanavir, dasatinib and erlotinib). If voriconazole is taken concomitantly with LANCAP the plasma concentration of both medicines may be increased.

HIV protease inhibitors:

It has been shown that co-administration of atazanavir with proton-pump inhibitors such as LANCAP results in a substantial reduction in the bioavailability of atazanavir. Therefore, LANCAP 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, may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Methotrexate:

Concomitant administration of methotrexate (particularly in high doses) with LANCAP may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydromethotrexate. However, no formal interaction studies of high dose methotrexate with PPIs such as LANCAP have been conducted (see section 4.4).

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Digoxin:

The absorption of digoxin may be enhanced if taken with LANCAP, resulting in increased plasma concentrations. Plasma levels of digoxin should thus be monitored and if necessary, the dosage adjusted upon initiating and ending LANCAP treatment.

Warfarin:

The response to anticoagulants such as warfarin may be affected by any concomitant medicine. It is therefore good practice to monitor the patient with additional PT (prothrombin time)/INR (international normalised ratio) determinations when LANCAP is initiated, discontinued or taken irregularly, since a minor reduction in the concentration of warfarin may occur.

Medicines metabolised by P450 enzymes

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

Theophylline:

LANCAP 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 is commenced or discontinued, to ensure clinically effective blood levels. Caution is thus advised when used in combination

Tacrolimus:

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

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Medicines transported by P-glycoprotein

Lansoprazole, as in LANCAP, 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

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, can reduce the plasma concentrations of lansoprazole.

Others

Sucralfate/Antacids

Administration of LANCAP concomitantly with sucralfate delays absorption of the proton pump inhibitor and reduces bioavailability by approximately 17 %. Therefore, LANCAP should be taken at least 30 minutes prior to sucralfate.

The administration of antacids and LANCAP does not interfere with its effect.

Non-steroidal anti-inflammatory medicines

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

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Since LANCAP is a weak inducer of the cytochrome P450 system, the possibility exists for interactions with medicines which are metabolized via this system, such as warfarin, antipyrine, indomethacin, ibuprofen, or other nonsteroidal anti-inflammatory medicines (NSAIDs); oral contraceptives, phenytoin, propranolol, prednisone, diazepam or clarithromycin.

The decrease in gastric activity with LANCAP may give false positive results in diagnostic investigations for neuroendocrine tumours and treatment should be stopped before such investigations.

Treatment with LANCAP may cause false-negative results in the urea breath test for *Helicobacter pylori* infection. It is recommended that a urea breath test should not be performed for at least 2 weeks after stopping treatment with LANCAP.

LANCAP has been shown to have no clinically significant interaction with amoxicillin.

Concomitant administration of LANCAP with clopidogrel in healthy patients has no clinically important effect on exposure to the active metabolite of clopidogrel or clopidogrel-induced platelet inhibition. No dose adjustment of clopidogrel is necessary when administered with an approved dose of LANCAP.

4.6 Fertility, pregnancy and lactation

Pregnancy

Adequate and well-controlled studies in humans have not been done (see section 4.3)

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Breastfeeding

It is not known whether lansoprazole is distributed into breast milk. However, lansoprazole or its metabolites are distributed into the milk of rats. Lansoprazole has been shown to cause tumourigenic effects in animals.

4.7 Effects on ability to drive and use machines

Caution is advised since LANCAP can influence the ability to drive and use machines (see section 4.8). Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects

Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Side effects**
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, anaemia, leukopenia, 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	Hypomagnesaemia, severe hypomagnesaemia can correlate with hypocalcaemia and may result in

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	Frequency unknown	hypokalaemia, hypocalcaemia, 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
Vascular disorders	Less frequent	Vasodilation, cerebrovascular accident/cerebral infarction, hypertension/hypotension, migraine, syncope
Respiratory, thoracic and	Less frequent	Asthma, bronchitis, cough increased, dyspnoea, epistaxis, haemoptysis, hiccough, laryngeal neoplasia,

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mediastinal disorders		pharyngitis, pleural disorder, pneumonia, respiratory disorder, upper respiratory inflammation/infection, rhinitis, sinusitis, stridor
Gastrointestinal disorders	Frequent Less frequent	Diarrhoea, dry mouth or throat, nausea, vomiting, constipation, abdominal pain, flatulence Abnormal stools, anorexia, bezoar, cardiospasm, 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,
Gastrointestinal disorders continued	Less frequent	Thirst, tongue disorder, ulcerative colitis, ulcerative stomatitis, pancreatitis (sometimes fatal)
Hepato-biliary disorders	Frequent Less frequent	Elevation in hepatic enzymes Hepatitis, jaundice, hyperbilirubinaemia

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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 carcinoma, skin disorder, sweating, Steven-Johnson syndrome or toxic-epidermal necrolysis, photosensitivity, petechiae, purpura
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
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, interstitial nephritis; in some patients, renal failure has been reported concomitantly (see section 4.4)
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
General disorders and administrative site conditions	Frequent Less frequent	Fatigue Asthenia, carcinoma, chest pain, chills, fever, flu syndrome, halitosis, infection, malaise, oedema, pain

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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 professionals 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 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, in humans are not known (although the acute toxicity is likely to be low) and, consequently, instructions for treatment cannot be given. 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.

See 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, is not significantly eliminated by haemodialysis.

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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 gastro-intestinal 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 to 1,5 hours.

Elimination:

The main route of elimination is via the bile with 15 – 30 % of lansoprazole being 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 to 100 %. Because the mean half-life in the elderly remains between 1,9 to 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 to 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 to 7,2 hours. An increase in mean 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.

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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.

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 Polyethylene glycol 6000

Polysorbate 80

Povidone K-30

Sodium lauryl sulphate

Sucrose

Sugar spheres

Talc

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

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6.4 Special precautions for storage

Store in a dry place at or below 30 ºC.

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

6.5 Nature and contents of container

LANCAP 15 mg capsules are available in white HDPE bottles closed with a polypropylene tamper-evident cap with mounted desiccant insert containing 7, 14, 28 or 30 capsules.

LANCAP 30 mg capsules are available in white HDPE bottles closed with a polypropylene tamper-evident cap with mounted desiccant insert containing 14, 28 or 30 capsules.

6.6 Special precautions for disposal

No special precautions.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

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8. REGISTRATION NUMBERS

LANCAP 15 mg: A40/11.4.3/0247

LANCAP 30 mg: A40/11.4.3/0248

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9. DATE OF FIRST AUTHORISATION

Date of registration: 02 March 2007

10. DATE OF REVISION OF THE TEXT

25 February 2026

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