**1.3.1.1.1 APPROVED PROFESSIONAL INFORMATION**

**SCHEDULING STATUS**

**S3**

## 1 NAME OF THE MEDICINE

**LOPRICID 100** tablets

**LOPRICID 300** tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

LOPRICID 100:

Each tablet of LOPRICID 100 contains 100 mg allopurinol.

Contains sugar: Lactose monohydrate 30,53 mg per tablet.

LOPRICID 300:

Each tablet of LOPRICID 300 contains 300 mg allopurinol.

Contains sugar: Lactose monohydrate 90,10 mg per tablet.

For full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Tablets

LOPRICID 100: White to off-white coloured, flat faced bevelled edged, round tablets, on one side debossed with “0” and “21” on either side of a scoreline and “100” on the other side.

LOPRICID 300: Peach coloured, flat faced bevelled edged, round tablets on one side Debossed with “300” and “020” on either side of a scoreline and plain on the other side.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

LOPRICID is indicated in adults:

- for the treatment of gout and hyperuricaemia associated with other conditions. It reduces the concentration of uric acid in plasma with gradual resolution of tophi and reduces the risk of the formation of uric acid calculi. It may be effective in patients with impaired renal function.
- in the treatment of hyperuricaemia associated with leukaemia or resulting from radiotherapy or the use of anti-neoplastic medicines such as mercaptopurine or during treatment with thiazides (e.g. hydrochlorothiazide).

**4.2 Posology and method of administration**

**Posology**

*Adults*

In gout, it is usual to commence with 50 mg twice daily and to increase this dose as required up to 200 mg to 400 mg daily in divided doses.

In severe conditions, daily doses of up to 900 mg may be necessary.

In hyperuricaemia associated with leukaemia a suggested initial dose is 200 mg three times daily commencing, if possible, 2 or 3 days before radiotherapy or the commencement of treatment with anti-neoplastic medicines, and adjusted as requested to a maintenance dose, usually of 300 mg to 400 mg daily.

**Instructions for use**

Fluid intake should be sufficient to maintain daily urinary volume above 2 litres.

LOPRICID is well tolerated, especially after food. Patients on high doses (> 300 mg) may benefit from a divided dose regimen.

**Special populations**

*Renal impairment*

Since LOPRICID and its metabolites are excreted by the kidney, impaired renal function may lead to retention of LOPRICID and/or its metabolites with consequent prolongation of plasma half-lives. In severe renal insufficiency, it may be advisable to use less than 100

mg per day or to use single doses of 100 mg at longer intervals than one day.

If facilities are available to monitor plasma oxipurinol concentrations, the dose should be adjusted to maintain plasma oxipurinol levels below 100 micromol/litre (15,2 mg/litre).

LOPRICID and its metabolites are removed by renal dialysis. If dialysis is required two to three times a week consideration should be given to an alternative dosage schedule of 300 mg to 400 mg LOPRICID immediately after each dialysis with none in the interim.

*Hepatic impairment*

Reduced doses should be used in patients with hepatic impairment. Periodic liver function tests are recommended during the early stages of therapy.

**Paediatric population**

For children, the suggested initial dose is 8 mg per kg body mass daily.

**Method of administration**

For oral administration.

### 4.3 Contraindications

LOPRICID is contraindicated in:

- Hypersensitivity to allopurinol or to any of the other ingredients of LOPRICID (see section 6.1).
- Pregnancy and breastfeeding (see section 4.6).
- Children, except those with malignancy.

### 4.4 Special warnings and precautions for use

*Hypersensitivity*

LOPRICID should be withdrawn immediately when a skin rash or other evidence of sensitivity occurs as this could result in more serious hypersensitivity reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis) (see sections 4.3 and 4.8).

Skin reactions are the most common reactions and may occur at any time during treatment. They may be pruritic, maculopapular, sometimes scaly, sometimes purpuric and rarely exfoliative, such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

LOPRICID should be withdrawn immediately should such reactions occur. After recovery from mild reactions, LOPRICID may, if desired, be re-introduced at a small dose (e.g. 50 mg/day) and gradually increased. If the rash recurs, LOPRICID should be permanently withdrawn as more severe hypersensitivity may occur (see section 4.8).

The clinical diagnosis of SJS/TEN remains the basis for decision making. If such reactions occur at any time during treatment, allopurinol should be withdrawn immediately and permanently.

Angioedema has been reported to occur with and without signs and symptoms of a more generalised hypersensitivity reaction.

Fever has been reported to occur with and without signs and symptoms of a more generalised LOPRICID hypersensitivity reaction (see section 4.8).

*HLA-B*5801 allele*

The HLA-B*5801 allele has been reported as a genetic risk factor for allopurinol associated SJS/TEN in retrospective, case-control, pharmacogenetic studies in patients of Han Chinese, Japanese and European descent. Up to 20 % to 30 % of some Han Chinese, African and Indian populations carry the HLA-B*5801 allele whereas only 1 % to 2 % of Northern European, US European and Japanese patients are estimated to be HLA-B*5801 carriers. However, the use of genotyping as a screening tool to make decisions about treatment with LOPRICID has not been established.

*Chronic renal impairment*

Patients with chronic renal impairment and concomitant diuretic use, in particular thiazides, may be at increased risk of developing hypersensitivity reactions including SJS/TEN associated with allopurinol. Extra vigilance for the signs of hypersensitivity syndrome or SJS/TEN is required and the patient should be informed of the need to stop treatment immediately and permanently at the first appearance of symptoms (see section 4.8).

*Hepatic and renal impairment*

Reduced doses should be used in patients with hepatic or renal impairment. LOPRICID should be used with caution in patients with hypertension and cardiac insufficiency treated with diuretics and ACE inhibitors.

Adverse reactions in association with LOPRICID are rare in the overall treated population and mostly of a minor nature. The incidence is higher in the presence of renal and/or hepatic disorder.

Hepatic dysfunction has been reported without overt evidence of more generalised hypersensitivity.

*Asymptomatic hyperuricaemia*

Asymptomatic hyperuricaemia is generally not considered an indication for use of LOPRICID. Fluid and dietary modification with management of the underlying cause may correct the condition.

*Acute gout attacks*

LOPRICID treatment should not be started until an acute attack of gout has completely subsided, as further attacks may be precipitated.

In the early stages of treatment with LOPRICID, an acute attack of gout arthritis may be precipitated. Therefore, it is advisable to give prophylaxis with a suitable anti-inflammatory

medicine or colchicine for at least one month.

If acute attacks develop in patients receiving LOPRICID, treatment should continue at the same dosage while the acute attack is treated with a suitable anti-inflammatory medicine.

*Xanthine deposition*

In conditions where the rate of urate formation is greatly increased (e.g. malignant disease and its treatment, Lesch-Nyhan syndrome) the absolute concentration of xanthine in urine could, in rare cases, rise sufficiently to allow deposition in the urinary tract. This risk may be minimised by adequate hydration to achieve optimal urine dilution.

*Impaction of uric acid renal stones*

Adequate therapy with LOPRICID will lead to dissolution of large uric acid renal pelvic stones, with the remote possibility of impaction in the ureter.

*Thyroid disorders*

Increased TSH values (> 5.5 µIU/mL) were reported in patients on long-term treatment with allopurinol. Caution is required when allopurinol is used in patients with alteration of thyroid function.

Thrombocytopenia, agranulocytosis and aplastic anaemia, particularly in individuals with impaired renal and/or hepatic function have been reported rarely, reinforcing the need for particular care in this group of patients.

Associated vasculitis and tissue response may be manifested in various ways including hepatitis, renal impairment and very rarely, seizures. Acute anaphylactic shock has been reported. If such reactions do occur, it may be at any time during treatment. LOPRICID should be withdrawn immediately and permanently.

Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions. When

generalised hypersensitivity reactions have occurred, renal and/or hepatic disorder has usually been present, particularly when the outcome has been fatal.

Angioimmunoblastic lymphadenopathy has been described following biopsy of a generalised lymphadenopathy. It appears to be reversible on withdrawal of LOPRICID.

Nausea and vomiting can be avoided by taking LOPRICID after meals.

*Excipients*

LOPRICID contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**4.5 Interaction with other medicines and other forms of interaction**

*6-mercaptopurine and azathioprine:* Azathioprine is metabolised to 6-mercaptopurine which is inactivated by the action of xanthine oxidase. When 6-mercaptopurine or azathioprine is given concurrently with LOPRICID, only one-quarter of the usual dose of 6-mercaptopurine or azathioprine should be given because inhibition of xanthine oxidase will prolong their activity.

*Vidarabine (adenine arabinoside):* Evidence suggests that the plasma half-life of vidarabine is increased in the presence of allopurinol. When these two products are used concomitantly caution is necessary, to recognise enhanced toxic effects.

*Salicylates and uricosuric medicines:* oxipurinol, the major metabolite of allopurinol and itself therapeutically active, is excreted by the kidney in a similar way to urate. Hence, medicines with uricosuric activity such as probenecid or large doses of salicylate may accelerate the excretion of oxipurinol. This may decrease the therapeutic activity of LOPRICID, but the significance of this needs to be assessed in each individual case.

*Chlorpropamide:* If LOPRICID is given concomitantly with chlorpropamide when renal function is poor, there may be an increased risk of prolonged hypoglycaemic activity, because allopurinol and chlorpropamide may compete for excretion in the renal tubule.
*Coumarin anticoagulants:* There have been reports of increased effect of warfarin and other coumarin anticoagulants when co-administered with allopurinol as in LOPRICID. Therefore, all patients receiving anticoagulants must be carefully monitored.

Phenytoin: LOPRICID 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 LOPRICID therapy.

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

*Cyclophosphamide, doxorubicin, bleomycin:* Enhanced bone marrow suppression by cyclophosphamide and other cytotoxic medicines has been reported among patients with neoplastic disease (other than leukaemia), in the presence of allopurinol, as contained in LOPRICID. However, it has been reported that patients treated with cyclophosphamide, doxorubicin and/or bleomycin, allopurinol, as contained in LOPRICID, did not appear to increase the toxic reaction of these cytotoxic medicines.

Blood dyscrasias occur more frequently than when these active substances are administered alone. Blood count monitoring should therefore be performed at regular intervals.

*Ciclosporin:* Plasma concentration of ciclosporin may be increased during concomitant treatment with LOPRICID. Enhanced ciclosporin toxicity should be considered if these medicines are co-administered.

*Didanosine:* In reported studies healthy volunteers and HIV patients receiving didanosine, plasma didanosine $C_{max}$ and AUC values were approximately doubled with concomitant allopurinol, as contained in LOPRICID, treatment (300 mg daily) without affecting terminal half-life. Co-administration of these two medicines is not recommended. If concomitant use is unavoidable, a dose reduction of didanosine may be required, and patients should be closely monitored.

*Diuretics:* An interaction between allopurinol and furosemide that results in increased serum urate and plasma oxipurinol concentrations has been reported. An increased risk of hypersensitivity has been reported when allopurinol is given with diuretics, in particular thiazides, especially in renal impairment.

*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.

**4.6 Fertility, pregnancy and lactation**

**Pregnancy**

LOPRICID is contraindicated in pregnancy (see section 4.3).

**Breastfeeding**

LOPRICID is contraindicated in lactation (see section 4.3).

**Fertility**

No data available.

### 4.7 Effects on ability to drive and use machines

Since adverse reactions such as somnolence, vertigo and ataxia have been reported in patients receiving allopurinol as contained in LOPRICID, patients should exercise caution before driving, using machinery or participating in dangerous activities until they are reasonably certain that LOPRICID does not adversely affect performance.

### 4.8 Undesirable effects

**a. Tabulated summary of adverse reactions**

| MedDRA system organ class | Frequency | Adverse reactions |
|---|---|---|
| Infections and infestations | Less frequent | Furunculosis |
| Blood and lymphatic system disorders | Less frequent | Leucopenia, leucocytosis, eosinophilia, haemolytic anaemia, agranulocytosis, aplastic anaemia, thrombocytopenia[1] |
| Immune system disorders | Less frequent | Hypersensitivity reactions[2] (including skin reactions associated with exfoliation, fever, lymphadenopathy, arthralgia, eosinophilia, Stevens-Johnson syndrome and toxic epidermal necrolysis), angioimmunoblastic lymphadenopathy[3], |

| **MedDRA system organ class** | **Frequency** | **Adverse reactions** |
|---|---|---|
| | | anaphylactic reaction, vasculitis |
| Metabolism and nutrition disorders | Less frequent | Diabetes mellitus, hyperlipidaemia |
| Psychiatric disorders | Less frequent | Depression, drowsiness |
| Nervous system disorders | Less frequent | Headache, peripheral neuritis, seizures, paraesthesia, coma, paralysis, ataxia, somnolence, dysgeusia |
| | Frequency unknown | Aseptic meningitis |
| Eye disorders | Less frequent | Cataract, visual disturbances, macular changes |
| Ear and labyrinth disorders | Less frequent | Vertigo |
| Cardiac disorders | Less frequent | Angina, bradycardia |
| Vascular disorders | Less frequent | Hypertension |
| Gastrointestinal disorders | Less frequent | Nausea[4], vomiting[4], abdominal pain, diarrhoea, gastric irritation, taste disturbances, recurrent haematemesis, steatorrhoea, stomatitis, changed bowel habit |
| Hepato-biliary disorders | Less frequent | Hepatic damage, hepatotoxicity, altered liver function, hepatitis (including hepatic necrosis and granulomatous hepatitis)[5] |
| Skin and subcutaneous | Frequent | Rash |

| MedDRA system organ class | Frequency | Adverse reactions |
|---|---|---|
| tissue disorders | Less frequent | Stevens-Johnson syndrome, toxic epidermal necrolysis[6], skin eruptions, exfoliative rash, alopecia, angioedema[7], discoloured hair |
| Musculoskeletal and connective tissue disorders | Less frequent | Arthralgia |
| Renal and urinary disorders | Less frequent | Renal damage, haematuria, uraemia, Azotaemia |
| Reproductive system and breast disorders | Less frequent | Gynaecomastia, male infertility, erectile dysfunction |
| General disorders and administration site conditions | Less frequent | Fever[8], chills, malaise, oedema, asthenia. |
| Investigations | Frequent | Blood thyroid stimulating hormone increased[9]. |

1 = Reports of thrombocytopenia, agranulocytosis and aplastic anaemia, particularly in individuals with impaired renal and/or hepatic function, reinforcing the need for particular care in this group of patients.

2 = A delayed multi-organ hypersensitivity disorder (known as hypersensitivity syndrome or DRESS) with fever, rashes, vasculitis, lymphadenopathy, pseudo lymphoma, arthralgia, leucopenia, eosinophilia hepato-splenomegaly, abnormal liver function tests, and vanishing bile duct syndrome (destruction and disappearance of the intrahepatic bile ducts) occurring in various combinations. Other organs may also be affected (e.g. liver, lungs, kidneys, pancreas, myocardium, and colon). If such reactions do occur, it may be at any time during treatment, allopurinol should be withdrawn IMMEDIATELY AND PERMANENTLY.

Rechallenge should not be undertaken in patients with hypersensitivity syndrome and

SJS/TEN. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions. When generalised hypersensitivity reactions have occurred, renal and/or hepatic disorder has usually been present particularly when the outcome has been fatal.

3 = Angioimmunoblastic T-cell lymphoma has been described very rarely following biopsy of a generalized lymphadenopathy. It appears to be reversible on withdrawal of allopurinol as in LOPRICID.

4 = In early reports, nausea and vomiting were reported. Further reports suggest that this reaction is not a significant problem and can be avoided by taking LOPRICID after meals.

5 = Hepatic dysfunction has been reported without overt evidence of more generalised hypersensitivity.

6 = Skin reactions are the most frequent reactions and may occur at any time during treatment. They may be pruritic, maculopapular, sometimes scaly, sometimes purpuric and rarely exfoliative, such as Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN). The highest risk for SJS and TEN, or other serious hypersensitivity reactions, is within the first weeks of treatment. The best results in managing such reactions come from early diagnosis and immediate discontinuation of any suspect medicine. LOPRICID should be withdrawn immediately should such reactions occur.

After recovery from mild reactions, LOPRICID may, if desired, be re-introduced at a small dose (e.g. 50 mg/day) and gradually increased. The HLA-8*5801 allele has been shown to be associated with the risk of developing allopurinol related hypersensitivity syndrome and SJS/TEN. The use of genotyping as a screening tool to make decisions about treatment with allopurinol has not been established. If the rash recurs, LOPRICID should be permanently withdrawn as more severe hypersensitivity may occur (see section 4.8 Immune system disorders). If SJS/TEN, or other serious hypersensitivity reactions cannot be ruled out, DO NOT re-introduce allopurinol due to the potential for a severe or even fatal reaction. The clinical diagnosis of SJS/TEN remains the basis for decision making. If such reactions occur at any time during treatment, allopurinol should be withdrawn immediately and permanently.

7 = Angioedema has been reported to occur with and without signs and symptoms of a more generalised hypersensitivity reaction.

8 = Fever has been reported to occur with and without signs and symptoms of a more generalised allopurinol hypersensitivity reaction (see section 4.8 Immune system disorders).

9 = The occurrence of increased thyroid stimulating hormone (TSH) did not report any impact on free T4 levels or had TSH levels indicative of subclinical hypothyroidism.

*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 SAHPRA website.

**4.9 Overdose**

**Symptoms**

Ingestion of up to 22,5 g allopurinol, as contained in LOPRICID, without adverse effect has been reported. Symptoms and signs including nausea, vomiting, diarrhoea and dizziness have been reported in a patient who ingested 20 g allopurinol.

**Treatment**

Treatment is symptomatic and supportive.

Recovery followed general supportive measures. Massive absorption of LOPRICID may lead to considerable inhibition of xanthine oxidase activity, which should have no untoward effects unless affecting concomitant medication, especially with 6-mercaptopurine and/or azathioprine. Adequate hydration to maintain optimum diuresis facilitates excretion of allopurinol, as contained in LOPRICID, and its metabolites. If considered necessary haemodialysis may be used.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Category and class: A 3.3 Anti-gout preparations

Pharmacotherapeutic Group: Antigout preparations inhibiting uric acid production ATC code: M04 AA01

*Mechanism of action*

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. In addition to the inhibition of purine catabolism in some but not all hyperuricaemic patients, de novo purine biosynthesis is depressed via feedback inhibition of hypoxanthine-guanine phosphoribosyltransferase. Other metabolites of allopurinol include allopurinol-riboside and oxipurinol-7 riboside.

### 5.2 Pharmacokinetic properties

**Absorption**

Allopurinol is active when given orally and is well absorbed from the upper gastrointestinal tract (duodenum and upper jejunum). Studies have detected allopurinol in the blood 30 to 60 minutes after dosing. Estimates of bioavailability vary from 67 % to 90 %. Peak plasma levels of allopurinol generally occur approximately 1,5 hours after oral administration of allopurinol but fall rapidly and are barely detectable after 6 hours. Peak levels of oxipurinol generally occur after 3 to 5 hours after oral administration of allopurinol and are much more sustained.

**Distribution**

Allopurinol is poorly bound by plasma proteins and therefore variations in protein binding are not thought to significantly alter clearance. The apparent volume of distribution of allopurinol is approximately 1,6 litre/kg which suggests relatively extensive uptake by tissues. Tissue concentrations of allopurinol have not been reported in humans, but it is

likely that allopurinol and oxipurinol will be present in the highest concentrations in the liver and intestinal mucosa where xanthine oxidase activity is high.

**Biotransformation**

The main metabolite of allopurinol is oxipurinol. Other metabolites of allopurinol include allopurinol-riboside and oxipurinol-7-riboside.

**Elimination**

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.

Oxipurinol is a less potent inhibitor of xanthine oxidase than allopurinol, but the plasma half-life of oxipurinol is far more prolonged. Estimates range from 13 to 30 hours in man. Therefore, effective inhibition of xanthine oxidase is maintained over a 24 hour period with a single daily dose of allopurinol. Patients with normal renal function will gradually accumulate oxipurinol until a steady-state plasma oxipurinol concentration is reached. Such patients, taking 300 mg of allopurinol per day will generally have plasma oxipurinol concentrations of 5 to 10 mg/litre.

Oxipurinol is eliminated unchanged in the urine but has a long elimination half-life because it undergoes tubular reabsorption. Reported values for the elimination half-life range from 13,6 hours to 29 hours. The large discrepancies in these values may be accounted for by variations in study design and/or creatinine clearance in the patients.

**Special populations**

**Renal impairment:**

Allopurinol and oxipurinol clearance is greatly reduced in patients with poor renal function resulting in higher plasma levels in chronic therapy. Patients with renal impairment, where

creatinine clearance values were between 10 and 20 mL/min, showed plasma oxipurinol concentrations of approximately 30 mg/litre after prolonged treatment with 300 mg allopurinol per day. This is approximately the concentration which would be achieved by doses of 600 mg/day in those with normal renal function. A reduction in the dose of allopurinol is therefore required in patients with renal impairment (see section 4.2).

**Elderly:**

The pharmacokinetics of the allopurinol are not likely to be altered other than due to deterioration in renal function (see Renal impairment).

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

LOPRICID 100:

- Anhydrous colloidal silica
- Crospovidone type B
- Isopropyl alcohol
- Lactose monohydrate
- Magnesium stearate
- Povidone PVP K30
- Pregelatinised starch
- Purified water

LOPRICID 300:

- Anhydrous colloidal silica
- Crospovidone type B
- Isopropyl alcohol
- FD&C Yellow no.6-aluminum lake (LAKE PIGMENT HT)
- Lactose monohydrate
- Magnesium stearate
- Povidone PVP K30

- Pregelatinised starch
- Purified water
-

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 Months

Store at or below 25 $^{0}$C.

Keep blisters in the outer carton until required for use.

### 6.4 Special precautions for storage

This medicine does not require any special storage conditions.

### 6.5 Nature and contents of container

LOPRICID 100 and LOPRICID 300:

30 or 100 tablets in a blister pack comprises of forming rigid PVC film and plain Alu lidding foil. Blisters are packed in an outer carton with a printed leaflet.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal <and other handling>

No special requirements.

## 7 HOLDER OF CERTIFICATE OF REGISTRATION

Trinity Pharma (Pty) Ltd

3 Gwen Lane

Fourth floor

Sandton

2031

Email: pv@trinitypharma.co.za

Contact number: +27 (0)10 594 5610

## 8 REGISTRATION NUMBER(S)

LOPRICID 100: 59/3.3/0761

LOPRICID 300: 59/3.3/0762

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14 July 2026

## 10 DATE OF REVISION OF THE TEXT

N/A