PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

BECLOP 75 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each BECLOP film-coated tablet contains clopidogrel bisulphate equivalent to clopidogrel 75 mg.

Contains sugar: lactose monohydrate 94,425 mg per tablet.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

Pink coloured, round, film-coated tablets with '**C4**' embossed on one side and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BECLOP is indicated for the reduction of atherothrombotic events as follows

Recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease

Reduction of atherosclerotic events (myocardial infarction, stroke, death due to vascular causes) in patients with a history of symptomatic atherosclerotic disease defined by ischaemic stroke (from 7 days until less than 6 months), myocardial

infarction (from few days until less than 35 days) or established peripheral arterial disease.

Acute coronary syndrome

For patients with non-ST-segment elevation acute coronary syndrome (unstable angina/non-Q-wave myocardial infarction [MI]) including patients who are to be managed medically and those who are to be managed with percutaneous coronary intervention (with or without stent) or CABG (coronary artery bypass graft), BECLOP in combination with ASA has been shown to decrease the rate of a combined endpoint of cardiovascular death, myocardial infarction (MI), or stroke as well as the rate of a combined endpoint of cardiovascular death, MI, stroke, or refractory ischaemia.

For patients with ST-segment elevation acute myocardial infarction, BECLOP in combination with ASA has been shown to reduce the rate of death from any cause and the rate of a combined endpoint of death, re-infarction, or stroke.

4.2 Posology and method of administration

Posology

Adults

Recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease

The recommended daily dose of BECLOP is 75 mg once daily.

Acute coronary syndrome

For patients with non-ST-segment elevation acute coronary syndrome (unstable angina/non-Q-wave MI), BECLOP should be initiated with a single 300 mg loading dose and then continued at 75 mg once daily. Aspirin (75 mg – 325 mg once daily) should be initiated and continued in combination with BECLOP.

For patients with ST-segment elevation acute myocardial infarction, the recommended dose of BECLOP is 75 mg once daily, administered in combination with aspirin, with or without thrombolytics. BECLOP may be initiated with or without a loading dose.

Pharmacogenetics

CYP2C19 poor metaboliser status is associated with diminished antiplatelet response to clopidogrel. An appropriate dose regimen for this patient population has not been established in clinical outcome trials.

Special populations

No dosage adjustment is necessary for elderly patients or patients with renal disease.

Method of administration

For oral use.

BECLOP may be given with or without food.

4.3 Contraindications

- Hypersensitivity to clopidogrel or to any of the excipients of BECLOP (see section 6.1).
- Active pathological bleeding such as peptic ulcer and intracranial haemorrhage.
- Safety and efficacy in patients below the age of 18 have not been established.
- Safety and efficacy in pregnancy and lactation have not been established (see section 4.6)
- BECLOP is contraindicated in severe liver impairment.

- BECLOP is contraindicated in thrombocytopenia and platelet dysfunction.
- Haemophilia, congenital or acquired, or history of acquired haemophilia related to clopidogrel.

4.4 Special warnings and precautions for use

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) HAS BEEN REPORTED TO OCCUR WITH CLOPIDOGREL DURING POST MARKETING EXPERIENCE. MOST CASES WERE REPORTED IN THE FIRST TWO WEEKS OF TREATMENT. PRESCRIBERS SHOULD ALSO WARN PATIENTS ABOUT THE SIGNS AND SYMPTOMS OF THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP).

Thrombotic thrombocytopenic purpura (TTP)

There has been reports of thrombotic thrombocytopenic purpura (TTP), following the use of clopidogrel, sometimes after a short exposure.The clinical diagnosis of TTP is characterised by the presence of thrombocytopenia, and microangiopathic haemolytic anaemia, associated with either neurological symptoms, renal dysfunction or fever. Due to the risk of fatal outcome, in the event of suspected thrombotic thrombocytopenic purpura, BECLOP should be stopped. The management of a patient with thrombotic thrombocytopenic purpura is complex. Early treatment with plasmapheresis is indicated in TTP.

Bleeding and haematological disorders

Due to the risk of bleeding and haematological undesirable effects, blood cell count determination and/or other appropriate testing should be promptly considered whenever such suspected clinical symptoms arise during the course of treatment (see section 4.8).

BECLOP should he used with caution in patients who may be at risk of increased bleeding from trauma, surgery or other pathological conditions associated with bleeding diathesis and in patients receiving treatment with acetylsalicylic acid (aspirin), NSAIDs (including COX-2 inhibitors), heparin, ~~or~~ glycoprotein IIb/IIIa inhibitors, selective serotonin reuptake inhibitors (SSRIs), or CYP2C19 strong inducers or other medicines associated with bleeding risk (see section 4.5). Patients should be monitored carefully for any signs of bleeding, including occult bleeding, especially during the first week of treatment and/or after invasive cardiac procedures or surgery. The concomitant administration of clopidogrel with warfarin is not recommended since it may increase the intensity of bleedings. If a patient is to undergo elective surgery and an anti-platelet effect is not desired, BECLOP should be discontinued 7 days prior to surgery.

BECLOP prolongs bleeding time and should be used with caution in patients who have lesions with a propensity to bleed such as gastro-intestinal ulcers and intra-ocular bleeding. Medicines that might induce such lesions (such as acetylsalicylic acid and NSAIDs) should be used with caution in patients taking BECLOP.

Patents should be told that it may take longer than usual to stop bleeding when they take BECLOP, and that they should report any unusual bleeding to their medical practitioner. Patients should inform medical practitioners and dentists that they are taking BECLOP before any surgery is scheduled and before any new medicine is taken. In view of the possible increased risk of bleeding, the concomitant administration of BECLOP with acetylsalicylic acid, heparin, warfarin or thrombolytics should be undertaken with caution (see section 4.5).

Clopidogrel, as in BECLOP produces irreversible inhibition of platelet aggregation for the life of the platelet, which is 7-10 days.

If a patient is to undergo elective surgery and an antiplatelet effect is not desired, BECLOP should be discontinued 7 days prior to surgery.

Spinal and epidural anaesthesia should not be administered to a patient taking clopidogrel or for 7 days thereafter. No lumber puncture should be done during these 7 days due to risk of haematoma formation following lumber puncture or spinal and epidural anaesthesia.

Recent ischemic stroke

In patients with recent transient ischaemic attack (TIA) or stroke, who are at high risk of recurrent ischaemic events, the combination of aspirin and clopidogrel as in BECLOP has not been shown to be more effective than BECLOP alone, but the combination has been shown to increase major bleeding. It is therefore recommended that such addition should be undertaken with caution.

In patients with acute myocardial infarction, BECLOP therapy should not be initiated within the first few days following myocardial infarction.

In view of the lack of data, BECLOP cannot be recommended in coronary artery by-pass graft (CABG) and acute ischaemic stroke (less than 7 days).

Acquired haemophilia

Acquired haemophilia has been reported following use of clopidogrel. In cases of confirmed isolated activated Partial Thromboplastin Time (aPTT) prolongation with or without bleeding, acquired haemophilia should be considered. Patients with a confirmed diagnosis of acquired haemophilia should be managed and treated by specialists, and clopidogrel, as in BECLOP, should be discontinued.

Cytochrome P450 2C19 (CYP2C19)

Pharmacogenetics

In patients who are poor CYP2C19 metabolisers, clopidogrel, as in BECLOP, at recommended doses forms less of the active metabolite of clopidogrel and has a smaller effect on platelet function. Tests are available to identify a patient's

CYP2C19 genotype; these tests can be used as an aid in determining therapeutic strategy (see section 4.2).

Since clopidogrel, as in BECLOP, is metabolised to its active metabolite partly by CYP2C19, use of medicines that inhibit the activity of this enzyme would be expected to result in reduced medicine levels of the active metabolite of clopidogrel. As a precaution concomitant use of strong or moderate CYP2C19 inhibitors should be discouraged (see section 4.5 and 5.2).

Use of medicines that induce the activity of CYP2C19 would be expected to result in increased medicine levels of the active metabolite of clopidogrel, as in BECLOP, and might potentiate the bleeding risk. As a precaution concomitant use of strong CYP2C19 inducers should be discouraged (see section 4.5).

Cross-reactions among thienopyridines

Patients should be evaluated for history of hypersensitivity to other thienopyridines (such as ticlopidine, prasugrel) since cross-reactivity among thienopyridines has been reported (see section 4.8). Thienopyridines may cause mild to severe allergic reactions such as rash, angioedema, or haematological cross-reactions such as thrombocytopaenia and neutropaenia. Patients who had developed a previous allergic reaction and/or haematological reaction to one thienopyridine may have an increased risk of developing the same or another reaction to another thienopyridine. Monitoring for signs of hypersensitivity in patients with a known allergy to thienopyridines is advised.

Renal- and hepatic impairment

As clinical experience is limited in patients with renal impairment and moderate hepatic disease with bleeding diatheses, BECLOP should be used with caution in these patients.

Thrombocytopenia, neutropenia, aplastic anaemia and pancytopenia have been reported in patients taking clopidogrel (see section 4.8).

Excipient warning

BECLOP contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g., galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take BECLOP.

BECLOP contains lactose monohydrate, which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

Medicines associated with bleeding risk

There is an increased risk of bleeding due to the potential additive effect. The concomitant administration of medicines associated with bleeding risk should be undertaken with caution (see section 4.4).

Acetylsalicylic acid (aspirin/ASA)

BECLOP potentiates the effects of acetylsalicylic acid on collagen-induced platelet aggregation. A pharmacodynamic interaction between clopidogrel and acetylsalicylic acid (aspirin) is possible, leading to increased risk of bleeding. Therefore, concomitant use should be undertaken with caution. The safety of the chronic concomitant administration of acetylsalicylic acid (aspirin) and BECLOP has not been established (see section 4.4). However, clopidogrel and ASA (75-325 mg once daily) have been administered together for up to one year.

Heparin

There have been reports that clopidogrel did not necessitate modification of the heparin dose or alter the effect of heparin on coagulation. Co-administration of heparin had no effect on the inhibition of platelet aggregation induced by clopidogrel. A pharmacodynamic interaction between clopidogrel and heparin is

possible, leading to increased risk of bleeding. The safety of this combination has not been established and concomitant use should be undertaken with caution (see section 4.4).

Thrombolytics

The safety of the concomitant administration of BECLOP, with other thrombolytic medicine has not been established and should be undertaken with caution.

Warfarin

The safety of the co-administration of BECLOP with warfarin has not been established. Consequently, the concomitant administration of these two medicines should be undertaken with caution, because of the increased risk of bleeding (see section 4.4).

Non-steroidal anti-inflammatory drugs (NSAIDs)

Data available indicates that the concomitant administration of clopidogrel and naproxen increased occult gastrointestinal blood loss. However, due to the lack of interaction studies with other NSAIDs, it is presently unclear whether there is an increased risk of gastrointestinal bleeding with all NSAIDs. Consequently, NSAIDs including COX-2 inhibitors and clopidogrel should be co-administered with caution (see section 4.4).

Glycoprotein IIb/IIIa inhibitors

BECLOP should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery or other conditions/disorders that may require concomitant glycoprotein IIb/IIIa inhibitors intake, as a pharmacodynamic interaction between clopidogrel and glycoprotein IIb/IIIa inhibitors is possible.

Selective serotonin reuptake inhibitors (SSRIs)

Since SSRIs affect platelet activation and increase the risk of bleeding, the concomitant administration of SSRIs with clopidogrel should be undertaken with caution.

Inhibitors of CYP1C19

Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicine that inhibit the activity of this enzyme would be expected to result in reduced medicine levels of the active metabolite of clopidogrel and a reduction in clinical efficacy. Concomitant use of strong or moderate CYP2C19 inhibitors should be discouraged (see section 4.4 and 5.2). Medicines that are strong or moderate CYP2C19 inhibitors include, for example, omeprazole and esomeprazole, fluvoxamine, fluoxetine, moclobemide, voriconazole, fluconazole, ticlopidine, carbamazepine, and efavirenz.

Inducers of CYP2C19

Since clopidogrel is metabolised to its active metabolite partly by CYP2C19, use of medicines that induce the activity of this enzyme would be expected to result in increased medicine levels of the active metabolite of clopidogrel.

Rifampicin strongly induces CYP2C19, resulting in both an increased level of clopidogrel active metabolite and platelet inhibition, which in particular might potentiate the risk of bleeding. As a precaution, concomitant use of strong CYP2C19 inducers should be discouraged (see section 4.4).

Proton pump inhibitors (PPI)

If a proton pump inhibitor is to be used concomitantly with BECLOP, consider using one with less CYP2C19 inhibitory activity.

Data available indicate that clopidogrel can be administered with pantoprazole. There is no evidence that other medicines that reduce stomach acid such as H2 blockers or antacids interfere with antiplatelet activity of clopidogrel.

Boosted anti-retroviral therapy (ART)

HIV patients treated with boosted anti-retroviral therapies (ART) are at high risk of vascular events.

A significantly reduced platelet inhibition has been shown in HIV patients treated with ritonavir-or cobicistat-boosted ART. Although the clinical relevance of these

findings is uncertain, there have been spontaneous reports of HIV-infected patients treated with ritonavir boosted ART, who have experienced re-occlusive events after de-obstruction or have suffered thrombotic events under a clopidogrel loading treatment schedule. Average platelet inhibition can be decreased with concomitant use of clopidogrel and ritonavir. Therefore, concomitant use of clopidogrel with ART boosted therapies should be discouraged.

Other concomitant therapy

No clinically significant pharmacodynamic interactions were observed when BECLOP was co-administered with atenolol, nifedipine, or both atenolol and nifedipine. The pharmacodynamic activity of BECLOP was not significantly influenced by the co-administration of phenobarbital, cimetidine or oestrogen.

The pharmacokinetics of digoxin or theophylline was not modified by the co-administration of BECLOP**.** Data available indicated that clopidogrel could inhibits the activity of one of the cytochromes P_{450} (CYP) enzymes, CYP 2C9. This could lead to increased plasma levels of medicines such as phenytoin, tolbutamide, warfarin, tamoxifen, fluvastatin and many NSAIDs which are metabolized by CYP 2C9.

CYP2C8 substrate medicines

Due to the risk of increased plasma concentrations, concomitant administration of clopidogrel and medicines primarily cleared by CYP2C8 metabolism (e.g., repaglinide, paclitaxel) should be undertaken with caution (see section 4.4).

4.6 Fertility, pregnancy, and lactation

Pregnancy

The use of BECLOP during pregnancy is not recommended as safety and efficacy have not been established.

Breastfeeding

The use of BECLOP during lactation is not recommended as safety and efficacy have not been established.

4.7 Effects on ability to drive and use machines

No impairment of driving or psychometric performance was observed following BECLOP administration.

4.8 Undesirable effects

a. Summary of the safety profile

The most reported adverse reaction during treatment was bleeding.

b. Tabulated summary of adverse reactions

Possibly related undesirable effects that have been reported in patients who received clopidogrel as in BECLOP, are listed in the table below. All known ADRs are listed by system organ class and frequency frequent, less frequent or frequency unknown.

System organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Frequent	Purpura
	Less frequent	Epistaxis, intracranial haemorrhage, severe neutropenia (including agranulocytosis), severe thrombocytopenia (including thrombotic thrombocytopenic purpura (TTP) (see section 4.4) and bruising, increased bleeding time,

System organ class	Frequency	Adverse reactions
		leucopenia, eosinophilia, aplastic anaemia[$], acquired haemophilia A.
	Frequency unknown	Haematuria, ocular bleeding (mainly conjunctival, but also ocular and retinal). gastro-intestinal haemorrhage, respiratory tract bleeding and aplastic anaemia (pancytopenia), musculoskeletal bleeding (including haemathrosis), haemorrhagic ulcer, haemothorax, haemorrhage of operative wound and retroperitoneal haemorrhage.
Immune system disorders	Frequency unknown	Hypersensitivity reactions such as bronchospasm, angioedema or anaphylactoid reactions, serum sickness, cross-reactive drug hypersensitivity among thienopyridines (such as ticlopidine, prasugrel).
Psychiatric disorders	Frequency unknown	Confusion, hallucinations
Nervous system disorders	Frequent	Dizziness, headache.
	Less frequent	Syncope, anxiety, paraesthesia,

System organ class	Frequency	Adverse reactions
		hypo-aesthesia, insomnia, mental depression, and intracranial bleeding.
	Frequency unknown	Taste disorders, ageusia
Eye disorders	Less frequent	Eye bleeding (mainly conjunctival, ocular, retinal)
Ear and labyrinth disorders	Less frequent	Vertigo
Cardiac disorders	Frequent	Chest pain.
	Less frequent	Atrial fibrillation or palpitations, oedema, hypertension.
	Frequency unknown	Kounis syndrome (vasospastic allergic angina)
Vascular disorders)	Frequent	Haematoma
	Frequency unknown	Hypotension, vasculitis.
Respiratory, thoracic, and mediastinal disorders	Frequent	Upper respiratory tract infections.
	Less frequent	Bronchitis, dyspnoea, cough.
	Frequency unknown	Interstitial pneumonitis, bronchospasm, eosinophilic pneumonia.
Gastrointestinal disorders	Frequent	Abdominal pain, dyspepsia
	Less frequent	Gastro-intestinal haemorrhage, diarrhoea, nausea, vomiting and

System organ class	Frequency	Adverse reactions
		gastric or duodenal ulcer.
	Frequency unknown	Flatulence and gastritis, constipation, colitis (including ulcerative or lymphocytic colitis), pancreatitis, stomatitis.
Hepato-biliary disorders	Frequency unknown	Abnormal liver function tests, hepatitis, acute liver failure.
Skin and subcutaneous tissue disorders	Less frequent	Pruritus, rash, severe skin reactions (including bullous eruption).
	Frequency unknown	Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalised exanthematous pustulosis (AGEP), drug-induced hypersensitivity syndrome, drug rash with eosinophilia and systemic symptoms (DRESS), *lichen planus*, urticaria, eczema.
Musculoskeletal, connective tissue and bone disorders	Frequent	Arthralgia, back pain, ~~T~~ tooth disorder.
	Less frequent	Gout, leg cramps.
	Frequency unknown	Myalgia, arthritis, arthralgia.
Renal and urinary disorders	Less frequent	Urinary tract infection, haematuria.

System organ class	Frequency	Adverse reactions
	Frequency unknown	Glomerulopathy, increased creatinine levels
Reproductive system and breast disorders	Less frequent	Gynaecomastia
General disorders and administration site conditions	Frequent	Generalised pain, flu-like symptoms, bleeding at the puncture site.
	Less frequent	Fatigue and asthenia.
	Frequency unknown	Fever
Investigations	Less frequent	Bleeding time prolonged, neutrophil count decreased; platelet count decreased

[$]These events related to myelotoxicity should be considered when a patient receiving BECLOP demonstrates fever or other signs of infection.

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Overdose following BECLOP administration may lead to prolonged bleeding time and subsequent bleeding complications. Appropriate therapy should be

considered if bleedings are observed. No antidote to the pharmacological activity of clopidogrel has been found. If prompt correction of prolonged bleeding time is required, platelet transfusion may reverse the effects of clopidogrel. Further treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 8.2 Anticoagulants.

Pharmacotherapeutic group platelet aggregation inhibitors excl. heparin, ATC Code B01AC-04.

Clopidogrel is a specific and potent inhibitor of platelet aggregation. It acts by irreversibly modifying the platelet ADP receptors. It inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor, and the subsequent ADP-mediated activation of the glycoprotein GP IIb/IIIa complex, thereby inhibiting platelet aggregation. Consequently, platelets exposed to clopidogrel are affected for the remainder of their lifespan and recovery of normal platelet function occurs at a rate consistent with platelet turnover (approximately 7 days).

Clopidogrel also inhibits platelet aggregation induced by other agonists by blocking the amplification of platelet activation by released ADP.

Biotransformation of clopidogrel is necessary to produce inhibition of platelet aggregation.

Repeated doses of 75 mg per day may produce inhibition of ADP-induced platelet aggregation from the first day; this may increase progressively and reached steady state between day 3 and day 7. At steady state, the average inhibition level observed with a dose of 75 mg per day was between 40 % and 60 %. Platelet aggregation and bleeding time gradually returned to baseline values, generally within 7 days after treatment was discontinued.

5.2 Pharmacokinetic properties

Absorption

After single and repeated oral doses, clopidogrel is rapidly absorbed. Mean peak plasma levels of unchanged clopidogrel (approximately 2,2 - 2,5 ng/ml after a single 75 mg oral dose) occurred approximately 45 minutes after dosing. Absorption is at least 50 % based on urinary excretion of clopidogrel metabolites.

Distribution

Clopidogrel and the main metabolite bind *in vitro* reversibly to human plasma proteins (98 % and 94 % respectively).

Biotransformation

Clopidogrel is extensively metabolised by the liver and the main metabolite.

In vitro and *in vivo*, clopidogrel is metabolised according to two main metabolic pathways one mediated by esterases and leading to hydrolysis into its inactive carboxylic acid derivative (85 % of circulating metabolites), and one mediated by multiple cytochromes P450. Clopidogrel is first metabolised to a 2-oxo-clopidogrel intermediate metabolite. Subsequent metabolism of the 2-oxo-clopidogrel intermediate metabolite results in formation of the active metabolite, a thiol derivative of clopidogrel. In vitro, this metabolic pathway is mediated by CYP3A4, CYP2C19, CYP1A2 and CYP2B6. The active thiol metabolite which has been isolated in vitro, binds rapidly and irreversibly to platelet receptors, thus inhibiting platelet aggregation.

Elimination

The elimination half-life of the main circulating metabolite may reach 8 hours after administration. Clopidogrel and the main metabolite are excreted in urine (50 %) and faeces (46 %).

Special population

Pharmacogenetics

CYP2C19 is involved in the formation of both the active metabolite and the 2-oxo-clopidogrel intermediate metabolite. Clopidogrel active metabolite pharmacokinetics and antiplatelet effects, differ according to CYP2C19 genotype. Tests are available to determine a patient's CYP2C19 genotype.

No substantial differences in active metabolite exposure and mean inhibition of platelet aggregation (IPA) were observed between ultrarapid, extensive, and intermediate metabolisers. In poor metabolisers, active metabolite exposure was decreased by 63 – 71 % compared to extensive metabolisers. Data shows that at steady state, platelet aggregation inhibition (5 µM ADP) was decreased in poor metabolisers with mean IPA of 37 % compared to 58 % in the extensive metabolisers and 60 % in the intermediate metabolisers.

There is some evidence that patients who are either intermediate or poor metabolisers may have a higher rate of cardiovascular events (death, myocardial infarction, stroke or stent thrombosis) compared to extensive metabolisers.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Hydrogenated castor oil

Lactose monohydrate

Low substituted hydroxypropyl cellulose (E463)

Macrogol 6 000

Microcrystalline cellulose

Tablet coating

Hypromellose (E464)

Iron oxide red (E172)

Macrogol

Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C in the original package, protected from light and moisture.

Do not remove the blister strips from the carton until required for use.

6.5 Nature and contents of container

Cartons contain 30 tablets packed in cold form blister strips. The blister strips are comprised of cold form blister laminate composed of aluminium foil (one side bright, soft tempered, plain; dull side lacquer laminated to oriented polyamide film; bright side lacquer laminated to PVC film), PVC and polyamide with a backing of aluminium foil coated with heat seal lacquer.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER

42/8.2/1086

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 March 2010

10 DATE OF REVISION OF THE TEXT

04 September 2022