PROFESSIONAL INFORMATION

SCHEDULING STATUS S4

1 NAME OF THE MEDICINE

ERCYTA 100 film-coated tablets

ERCYTA 150 film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ERCYTA 100

Each film-coated tablet contains erlotinib hydrochloride equivalent to 100 mg erlotinib.

ERCYTA 150

Each film-coated tablet contains erlotinib hydrochloride equivalent to 150 mg erlotinib.

Contains sugar (lactose monohydrate).

Excipients with known effect

ERCYTA 100

Each 100 mg film-coated tablet contains 72 mg lactose monohydrate.

ERCYTA 150

Each 150 mg film-coated tablet contains 108 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

ERCYTA 100

White to yellowish, round, biconvex, bevel-edged, coated tablets debossed with ‘ERL’ on one side and “100” on the other side.

ERCYTA 150

White to yellowish, round, biconvex, bevel-edged, coated tablets debossed with ‘ERL’ on one side and “150” on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Non-small cell lung cancer (NSCLC)

ERCYTA is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) activating mutation after failure of at least one prior chemotherapy regimen. ERCYTA was not effective after platinum-based therapy that included gemcitabine.

ERCYTA monotherapy is indicated for the maintenance treatment of patients having received first-line platinum-based (other than gemcitabine + cisplatin) doublets chemotherapy for locally advanced or metastatic NSCLC.

No survival benefit or other clinically relevant effects of the treatment have been demonstrated in patients with EGFR-negative tumours. See section 5.1.

Bronchial adenocarcinoma

ERCYTA is indicated for the first-line treatment of patients with locally advanced or metastatic (stage 4) bronchial adenocarcinoma whose tumours have demonstrated EGFR activating mutations and who have never smoked and had ECOG performance status of 0 – 1.

When prescribing ERCYTA, factors associated with prolonged survival should be considered.

No survival benefit or other clinically relevant effects of the treatment have been demonstrated in patients with EGFR-negative tumours. See section 5.1.

Pancreatic cancer

ERCYTA in combination with gemcitabine is indicated for the first-line treatment of patients diagnosed with locally advanced, unresectable or metastatic pancreatic cancer.

4.2 Posology and method of administration

Posology

ERCYTA treatment should be supervised by a medical practitioner who has experience in the use of anticancer therapies.

Concomitant use of CYP3A4 substrates and modulators may require dose adjustment (see section 4.5). Where dose adjustment is necessary, reduce in 50 mg steps.

Non-small cell lung cancer

EGFR mutation testing should be performed prior to initiation of ERCYTA therapy in chemo-naive patients with advanced or metastatic NSCLC and bronchial adenocarcinoma.

The recommended dose is one 150 mg tablet daily taken at least 1 hour before or two hours after the ingestion of food. Where dose adjustment is necessary, reduce in 50 mg steps.

Pancreatic cancer

The recommended daily dose of ERCYTA is 100 mg, taken at least one hour before or two hours after the ingestion of food, in combination with gemcitabine (see gemcitabine professional information for pancreatic cancer indication).

Hepatic impairment

Erlotinib is eliminated by hepatic metabolism and biliary excretion.

Erlotinib exposure was shown to be similar in patients with moderately impaired hepatic function (Child-Pugh score 7 – 9) compared with patients with adequate hepatic function, caution should however be used when administering ERCYTA to patients with hepatic impairment. See section 5.2. ERCYTA should not be used in patients with severe hepatic dysfunction (AST/SGOT and ALT/SGPT > 5 x ULN). Dose reduction or interruption of ERCYTA should be considered if severe adverse reactions occur.

Safety and efficacy have not been studied in patients with severe hepatic impairment.

Renal impairment

The safety and efficacy of ERCYTA has not been studied in patients with renal impairment (see section 5.2). ERCYTA should not be used in patients with severe renal impairment.

Paediatric use

The safety and efficacy of ERCYTA has not been established in patients under the age of 18 years (see section 5.2).

Tobacco smokers

Cigarette smoking has been shown to reduce erlotinib exposure by 50 to 60 %. The maximum tolerated dose of ERCYTA in NSCLC and bronchial adenocarcinoma patients who currently smoke cigarettes was 300 mg. The 300 mg dose did not show improved efficacy in second line treatment after failure of chemotherapy compared to the 150 mg dose in patients who continue to smoke cigarettes.

Method of administration

ERCYTA should be taken at least one hour before or two hours after the ingestion of food.

4.3 Contraindications

Hypersensitivity to erlotinib or to any of the excipients of ERCYTA listed in section 6.1.

4.4 Special warnings and precautions for use

Assessment of EGFR mutation status

When considering the use of ERCYTA as a first-line or maintenance treatment for locally advanced or metastatic NSCLC, it is important that the EGFR mutation status of a patient is determined.

A validated, robust, reliable and sensitive test with a prespecified positivity threshold and demonstrated utility for the determination of EGFR mutation status, using either tumour DNA derived from a tissue sample or circulating free DNA (cfDNA) obtained from a blood (plasma) sample, should be performed according to local medical practice.

If a plasma-based cfDNA test is used and the result is negative for activating mutations, perform a tissue test wherever possible due to the potential for false negative results from a plasma-based test.

Interstitial lung disease

Cases of interstitial lung disease (ILD)-like events, including fatalities, have been reported in patients receiving erlotinib, as in ERCYTA, for treatment of NSCLC, pancreatic cancer or other advanced solid tumours.

Reported diagnosis in patients suspected of having ILD-like events included pneumonitis, radiation pneumonitis, hypersensitivity pneumonitis, interstitial pneumonia, interstitial lung disease, obliterative bronchiolitis, pulmonary fibrosis, acute respiratory distress syndrome (ARDS), alveolitis and lung infiltration. Symptoms may start from a few days to several months after initiating ERCYTA therapy. Confounding or contributing factors such as

concomitant or prior chemotherapy, prior radiotherapy, pre-existing parenchymal lung disease, metastatic lung disease, or pulmonary infections were frequent.

In patients who develop acute onset of new or progressive pulmonary symptoms, such as dyspnoea, cough and fever, ERCYTA therapy should be interrupted pending diagnostic evaluation. If ILD is diagnosed, ERCYTA should be discontinued and appropriate treatment administered as necessary (see section 4.8).

Diarrhoea, dehydration, electrolyte imbalance and renal failure

Diarrhoea (including cases with a fatal outcome) has occurred in approximately 50 % of patients. Moderate or severe diarrhoea should be treated, e.g. with loperamide. In some cases, a dose reduction may be necessary.

Should persistent diarrhoea, nausea, anorexia, or vomiting associated with dehydration occur, ERCYTA therapy should be interrupted and appropriate measures should be taken to treat the dehydration (see section 4.8).

There have been reports of hypokalaemia and renal failure (including fatalities). Some cases were secondary to severe dehydration due to diarrhoea, vomiting and/or anorexia, while others were confounded by concomitant chemotherapy. In more severe or persistent cases of diarrhoea, or cases leading to dehydration, particularly in groups of patients with aggravating risk factors (especially concomitant chemotherapy and other medications, symptoms or diseases or other predisposing conditions including advanced age), ERCYTA therapy should be interrupted and appropriate measures should be taken to intensively rehydrate the patients intravenously. In addition, renal function and serum electrolytes including potassium should be monitored in patients at risk of dehydration.

Hepatitis and hepatic failure

Cases of hepatic failure (including fatalities) have been reported during use of ERCYTA. Confounding factors have included pre-existing liver disease or concomitant hepatotoxic medications. Therefore, in such patients, periodic liver function testing should be

considered. ERCYTA dosing should be interrupted if changes in liver function are severe (see section 4.8). ERCYTA is not recommended for use in patients with severe hepatic dysfunction.

Gastrointestinal perforation

Patients receiving ERCYTA are at increased risk of developing gastrointestinal perforation (including some cases with a fatal outcome). Patients receiving concomitant anti-angiogenic medicines, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) and/or taxanes, or who have prior history of peptic ulceration or diverticular disease are at increased risk. ERCYTA should be permanently discontinued in patients who develop gastrointestinal perforation (see section 4.8).

Bullous and exfoliative skin disorders

Bullous, blistering and exfoliative skin conditions have been reported, including cases suggestive of Stevens-Johnson syndrome/toxic epidermal necrolysis (TEN), which in some cases were fatal (see section 4.8).

ERCYTA treatment should be interrupted or discontinued if the patient develops severe bullous, blistering or exfoliating conditions. Patients with bullous and exfoliative skin disorders should be tested for skin infection and treated.

Ocular disorders

Cases of corneal perforation or ulceration, uveitis, iridocyclitis and iritis have been reported during use of ERCYTA (see section 4.8).

Other ocular disorders including abnormal eyelash growth, keratoconjunctivitis sicca or keratitis have been observed with ERCYTA treatment, which are also risk factors for corneal perforation/ulceration.

Patients presenting with signs and symptoms suggestive of keratitis should be referred promptly to an ophthalmologist.

If a diagnosis of ulcerative keratitis is confirmed, treatment with ERCYTA should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered.

ERCYTA should be used with caution in patients with a history of keratitis, ulcerative keratitis or severe dry eye. Contact lens use is a further risk factor for keratitis and ulceration.

Tobacco smokers

Efficacy in smoking or previous or past-smoking patients has not been established (see section 4.5).

Current smokers should be advised to stop smoking, as plasma concentrations of erlotinib in smokers, as compared to non-smokers are reduced (see section 5.2).

Interactions with other medicines

ERCYTA has a potential for clinically significant medicine interactions (see section 4.5).

Special warnings regarding excipients

ERCYTA contains lactose.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take ERCYTA.

4.5 Interactions with other medicines and other forms of interactions

CYP substrates

Erlotinib, as in ERCYTA, is a potent inhibitor of CYP1A1 and a moderate inhibitor of CYP3A4 and CYP2C8. Furthermore, erlotinib is a strong inhibitor of glucuronidation by the uridine diphosphate glucuronosyltransferase isoenzyme UGT1A1 *in vitro.* The physiological relevance of the strong inhibition of CYP1A1 is unknown due to the very limited expression of CYP1A1 in human tissues.

When erlotinib was co-administered with ciprofloxacin, a moderate CYP1A2 inhibitor, the erlotinib exposure [AUC] increases significantly with no statistically significant change in C_{max}. Similarly, the exposure to the active metabolite increases significantly. The clinical relevance of this increase has not been established. Caution should be exercised when ciprofloxacin or potent CYP1A2 inhibitors (e.g. fluvoxamine) are combined with ERCYTA. If adverse events related to erlotinib are observed, the dose of ERCYTA may be reduced.

Pre-treatment or co-administration of ERCYTA does not alter the clearance of the prototypical CYP3A4 substrates, midazolam and erythromycin, but appear to decrease the oral bioavailability of midazolam by up to 24 %. Erlotinib was shown not to affect pharmacokinetics of the concomitantly administered CYP3A4/2C8 substrate paclitaxel. Significant interactions with the clearance of other CYP3A4 substrates are therefore unlikely.

The inhibition of glucuronidation may cause interactions with medicines which are substrates of UGT1A1 and exclusively cleared by this pathway. Patients with low expression levels of UGT1A1 or genetic glucuronidation disorders (e.g. Gilbert's disease) may exhibit increased serum concentrations of bilirubin and should be treated with caution.

Erlotinib is metabolised in the liver, primarily by CYP3A4 and to a lesser extent by CYP1A2. Extrahepatic metabolism by CYP3A4 in intestine, CYP1A1 in lung, and CYP1B1 in tumour tissue also potentially contribute to the metabolic clearance of erlotinib. Potential interactions may occur with active substances metabolised by, or that are inhibitors or inducers of, these enzymes.

Potent inhibitors of CYP3A4 activity decrease erlotinib metabolism and increase erlotinib plasma concentrations. Concomitant use of erlotinib, as in ERCYTA, with ketoconazole (a potent CYP3A4 inhibitor) results in a significant increase of erlotinib exposure. Therefore, caution should be used when erlotinib is combined with a potent CYP3A4 inhibitor or combined CYP3A4 / CYP1A2 inhibitor, e.g. azole antifungal medicines (i.e. ketoconazole,

itraconazole, voriconazole), protease inhibitors, erythromycin or clarithromycin. If necessary, the dose of ERCYTA should be reduced, particularly if toxicity is observed.

Potent inducers of CYP3A4 activity increase erlotinib metabolism and significantly decrease erlotinib plasma concentrations. Concomitant use of ERCYTA and rifampicin, a potent CYP3A4 inducer, can result in a significant decrease in erlotinib exposure. Co-administration of ERCYTA with CYP3A4 inducers should therefore be avoided. For patients who require concomitant treatment with ERCYTA and a potent CYP3A4 inducer such as rifampicin an increase in dose to 300 mg should be considered while their safety (including renal and liver functions and serum electrolytes) is closely monitored, and if well tolerated for more than 2 weeks, further increase to 450 mg could be considered with close safety monitoring.

Reduced exposure may also occur with other inducers e.g. phenytoin, carbamazepine, barbiturates or St. John's Wort (*Hypericum perforatum*). Caution should be observed if used concomitantly with ERCYTA. Alternative treatments lacking potent CYP3A4 inducing activity should be considered when possible.

Coumarin-derived anticoagulants

Increased International Normalised Ratio (INR) and bleeding events, which in some cases were fatal, have been reported in patients receiving concomitant coumarin-derived anticoagulants including warfarin. See section 4.4 and 4.8. Patients taking coumarin-derived anticoagulants should be monitored regularly for changes in prothrombin time or INR.

Statins

The combination of ERCYTA and a statin may increase the potential for statin-induced myopathy, including rhabdomyolysis.

Tobacco smoking

Cigarette smoking, which induces CYP1A1 and CYP1A2, has been shown to reduce erlotinib exposure by 50 – 60 %. Exposure to erlotinib is therefore significantly reduced compared to non-smokers (see section 5.2).

Efficacy in smoking patients has not been established.

Patients who are smoking should be advised to stop smoking.

P-glycoprotein inhibitors

Erlotinib is a substrate for the P-glycoprotein (Pgp) active substance transporter. Concomitant administration of inhibitors of Pgp, e.g. ciclosporin and verapamil, may lead to altered distribution and/or altered elimination of erlotinib. The consequences of this interaction for e.g. CNS toxicity have not been established. Caution should be exercised in such situations.

Medicines affecting gastrointestinal pH

Erlotinib is characterised by a decrease in solubility at pH above 5.

Medicines that increase the pH of the gastrointestinal (GI) tract, such as antacids, H_2-receptor antagonists, or proton pump inhibitors may therefore alter the solubility of erlotinib and hence its bioavailability. Increasing the dose of ERCYTA when co-administered with such medicines is not likely to compensate for this loss of exposure.

The effect of antacids and H_2 antagonists on the absorption of erlotinib have not been investigated but absorption may be impaired, leading to lower plasma levels. Combination of ERCYTA with proton pump inhibitors should be avoided. The effects of concomitant administration of erlotinib with H_2 antagonists and antacids are unknown; however, reduced bioavailability is likely. Therefore, concomitant administration of these combinations should be avoided. If the use of antacids is considered necessary during treatment with ERCYTA, they should be taken at least 4 hours before or 2 hours after the daily dose of ERCYTA.

If the use of ranitidine is considered, it should be used in a staggered manner, i.e. ERCYTA must be taken at least 2 hours before or 10 hours after the ranitidine dosing. The ranitidine dose should be divided into two equal doses per day.

Concomitant use with other chemotherapeutic medicines

There are no significant effects of gemcitabine on the pharmacokinetics of erlotinib. Conversely, there are no significant effects of erlotinib on the pharmacokinetics of gemcitabine.

Erlotinib increases platinum concentrations. The increase is not considered to be clinically relevant. In clinical practice, there may be other co-factors leading to an increased exposure to carboplatin like renal impairment. There were no significant effects of carboplatin or paclitaxel on the pharmacokinetics of erlotinib.

Capecitabine may increase erlotinib concentrations. When erlotinib was given in combination with capecitabine, there was a statistically significant increase in erlotinib AUC and a borderline increase in C_{max} when compared with values observed when erlotinib was given as monotherapy. There are no significant effects of erlotinib on the pharmacokinetics of capecitabine.

Due to the working mechanism, proteasome inhibitors including bortezomib may be expected to influence the effect of EGFR inhibitors including erlotinib. Such influence is supported by limited clinical data and preclinical studies showing EGFR degradation through the proteasome.

4.6 Fertility, pregnancy and lactation

Women who are pregnant and/or breastfeeding should not receive ERCYTA.

Pregnancy

There are no data available on the use of erlotinib, as in ERCYTA, in pregnant women. Studies in animals have shown reproductive toxicity.

Women of childbearing potential

Women of childbearing potential should be advised to avoid pregnancy while on ERCYTA. Adequate contraceptive methods should be used during therapy, and for at least 2 weeks after completing therapy.

Breastfeeding

It is not known whether erlotinib is excreted in human milk.

Mothers should be advised against breastfeeding while taking ERCYTA and for at least 2 weeks after the final dose.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed; however, erlotinib ERCYTA is not associated with impairment of mental ability.

4.8 Undesirable effects

System organ class **Frequency**	**Adverse reaction**
Infections and infestations	
Frequent:	Infections, with or without neutropenia, including pneumonia, sepsis and cellulitis
Metabolism and nutrition disorders	
Frequent:	Anorexia, decreased weight
Frequency unknown:	Hypokalaemia
Psychiatric disorders	
Frequent:	Depression
Nervous system disorders	
Frequent:	Neuropathy, headache

Eye disorders:

Frequent:	Keratoconjunctivitis sicca, keratitis, conjunctivitis
Less frequent:	Eyelash changes (including in-growing eyelashes, excessive growth and thickening of eyelashes), corneal perforation or ulceration (see section 4.4), uveitis.

Respiratory, thoracic and mediastinal disorders

Frequent:	Epistaxis, dyspnoea, cough
Less frequent:	Serious ILD, including fatalities (see section 4.4)

Gastrointestinal disorders

Frequent:	Diarrhoea, nausea, vomiting, stomatitis, abdominal pain, dyspepsia, flatulence, gastrointestinal bleeding, sometimes fatal
Less frequent:	Gastrointestinal perforation, sometimes fatal (see section 4.4)

Hepatobiliary disorders

Frequent:	Liver function test abnormalities (including increased alanine aminotransferase [ALT], aspartate aminotransferase [AST], bilirubin). These were mainly mild or moderate in severity, transient in nature or associated with liver metastases.
Less frequent:	Hepatitis, hepatic failure (including fatalities). Confounding factors have included pre-existing liver disease or concomitant hepatotoxic medicines (see section 4.4)

Skin and subcutaneous tissue disorders

Frequent:	Rash (erythematous, papulopustular), alopecia, pruritus, dry skin, paronychia, folliculitis, acne/ dermatitis acneiform, skin fissures
Less frequent:	Hirsutism, eyebrow changes, brittle and loose nails, hyperpigmentation, palmar-plantar erythrodysaesthesia syndrome,

	Stevens-Johnson syndrome, toxic epidermal necrolysis including fatalities (see section 4.4)
Renal and urinary disorders	
Frequent:	Renal insufficiency
Less frequent:	Nephritis, proteinuria
Frequency unknown:	Renal failure (including fatalities; see section 4.4)
General disorders and administration site conditions	
Frequent:	Fatigue, pyrexia, rigors

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 on the SAHPRA website: www.sahpra.org.za.

4.9 Overdose

Severe adverse reactions such as diarrhoea, rash and possibly liver transaminase elevation may occur above the recommended dose of 150 mg.

In case of suspected overdose ERCYTA should be withheld and symptomatic treatment initiated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 26 Cytostatic agents

Pharmacotherapeutic group: antineoplastic agent protein kinase inhibitor. ATC code: L01XE03.

Erlotinib inhibits the intracellular phosphorylation of HER1/EGFR (epidermal growth factor receptor type 1, also known as HER1). HER1/EGFR is expressed on the cell surface of normal cells and cancer cells. In non-clinical models, inhibition of EGFR phosphotyrosine results in cell stasis and/or death.

5.2 Pharmacokinetic properties

Absorption

After oral administration erlotinib has an extended absorption phase, with mean peak plasma levels occurring at approximately 4 hours after oral dosing.

Oral bioavailability is approximately 59 % compared to IV administration. The exposure after an oral dose may be increased by food.

Following absorption, erlotinib is highly bound in blood, with approximately 95 % bound to blood components, primarily to plasma proteins (i.e. albumin and alpha-1 acid glycoprotein [AAG]), with a free fraction of approximately 5 % at the recommended dose.

After an oral dose of 150 mg erlotinib, at steady state, the median time to reach maximum plasma concentrations is approximately 4,0 hours, with median maximum plasma concentrations achieved of 1,995 ng/ml. Prior to the next dose at 24 hours, the median minimum plasma concentrations are 1,238 ng/ml. Median AUC achieved during the dosing interval at steady state are 41,300 µg*h/ml.

Distribution

Erlotinib has a mean apparent volume of distribution of 232 liter and erlotinib distributes into tumour tissue of humans. Plasma protein binding is approximately 95 %. Erlotinib binds to serum albumin and alpha-1 acid glycoprotein (AAG).

Biotransformation

Erlotinib is metabolised in humans by the hepatic cytochrome P450 enzymes, primarily CYP3A4, and to a lesser extent by CYP1A2. Extrahepatic metabolism by CYP3A4 in the intestine, CYP1A1 in lung and CYP1B1 in tumour tissue potentially contribute to the metabolic clearance of erlotinib.

Three main metabolic pathways have been identified:

1. O-demethylation of either side chain or both, followed by oxidation to the carboxylic acids,
2. oxidation of the acetylene moiety followed by hydrolysis to the aryl carboxylic acid and
3. aromatic hydroxylation of the phenyl-acetylene moiety.

The primary metabolites of erlotinib produced by O-demethylation of either side chain have comparable potency to erlotinib. They are present at levels that are less than 10 % of erlotinib and display similar pharmacokinetics as erlotinib.

Elimination

The metabolites and trace amounts of erlotinib are mainly excreted via the faeces (> 90 %), with only a small amount of an oral dose eliminated via the kidneys.

The time to reach steady state plasma concentration is approximately 7 to 8 days. No significant relationships between predicted apparent clearance and patient age, body weight and gender occur.

Patient factors, which correlate with erlotinib pharmacokinetics, are serum total bilirubin, AAG concentrations and current smoking. Increased serum concentrations of total bilirubin and AAG concentrations are associated with a slower rate of erlotinib clearance; smokers had a higher rate of erlotinib clearance.

Co-administration of gemcitabine had no effect on erlotinib plasma clearance.

Pharmacokinetics in special populations

There have been no specific studies in paediatric or elderly patients.

Hepatic impairment

Erlotinib is primarily cleared by the liver. Erlotinib exposure was shown to be similar in patients with moderately impaired hepatic function (Child-Pugh score 7 – 9) compared with patients with adequate hepatic function, including patients with primary liver cancer or hepatic metastases.

Renal impairment

Erlotinib and its metabolites are not significantly excreted by the kidneys; less than 9 % of a single dose of erlotinib is excreted in the urine. No data are available in patients with compromised renal function.

Smokers

Studies have shown that cigarette smoking leads to increased clearance of, and decreased exposure to, erlotinib. The $AUC_{0\text{-infinity}}$ in smokers was about 1/3 of that in never/former smokers. This reduced exposure in current smokers is presumably due to induction of CYP1A1 in lung and CYP1A2 in the liver. See section 4.4, 4.5 and 4.2.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Microcrystalline cellulose, sodium starch glycolate, sodium lauryl sulphate, magnesium stearate, lactose monohydrate.

Tablet coating

Opadry white (consisting of titanium dioxide (E171), hydroxypropyl cellulose (E463), hydroxypropyl methylcellulose (E464) and polyethylene glycol (E1521)).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C in the original packaging (keep blisters in the carton until required for use and keep the bottle tightly closed).

6.5 Nature and contents of container

Container: Plastic, white, round HDPE bottles with a white round polypropylene cap with fine ribs at the lateral side, in a cardboard carton.

Blister: A rigid, transparent PVC film and aluminium foil in a push-through blister.

Packs of 30 or 100 tablets

Not all pack sizes are necessarily marketed at any one time.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATES OF REGISTRATION

Viatris South Africa (Pty) Ltd

4 Brewery Street, Isando

Gauteng

8 REGISTRATION NUMBERS

ERCYTA 100: 51/26/0127

ERCYTA 150: 51/26/0128

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

19 May 2022

10 DATE OF REVISION OF TEXT

26 January 2022