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SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ENORTERIB 500 mg (Film-coated tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ENORTERIB 500 mg: Each film-coated tablet contains abiraterone acetate 500 mg. Contains sugar: 245,45 mg lactose monohydrate per tablet.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Brownish pink, oval-shaped, film coated tablets debossed with 'G' one side and '121' on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ENORTERIB in combination with low-dose corticosteroids (prednisone or prednisolone) is indicated for the treatment of metastatic advanced prostate cancer (castration resistant prostate cancer) in adult male patients who have received prior chemotherapy containing docetaxel.

4.2 Posology and method of administration

Posology:

The recommended dose of **ENORTERIB** is 1 g (2x 500 mg tablets) as a single daily dose that **must not be taken with food**.

Taking **ENORTERIB** with food increases the systemic exposure to abiraterone (see *sections 4.5* and *5.2*).

Patients should be maintained on **ENORTERIB** until radiographic, symptomatic/ clinical progression and prostate-specific antigen (PSA) progression is confirmed (25 % increase over the patient's baseline/ nadir).

Dosage of prednisone or prednisolone:

For metastatic castration-resistant prostate cancer (mCRPC), **ENORTERIB** is used with 10 mg prednisone or prednisolone daily.

Recommended monitoring:

Serum transaminases and bilirubin should be measured prior to starting treatment with **ENORTERIB**, every 2 weeks for the first 3 months of treatment and monthly thereafter. Blood pressure, serum potassium and fluid retention should be monitored monthly (see *section 4.4*).

In the event of a missed daily dose of either **ENORTERIB**, prednisone or prednisolone, treatment should be resumed the following day with the usual daily dose.

Special Populations:

Hepatic impairment:

No dose adjustment is necessary for patients with pre-existing mild hepatic impairment (Child-Pugh class A). There are no data on the clinical safety and efficacy of multiple doses of abiraterone when administered to patients with moderate or severe hepatic impairment (Child Pugh Class B or C). No dose adjustment can be predicted.

ENORTERIB should not be used in patients with moderate or severe hepatic impairment (Child-Pugh class B or C) (see *sections 4.3* and *5.2*).

For patients who develop hepatotoxicity during **ENORTERIB** treatment, (alanine aminotransferase (ALT) or aspartate aminotransaminase (AST) increases > 5 times the upper limit of normal (ULN) or bilirubin increases > 3 x ULN), treatment should be withheld immediately until liver function tests are back to pre-treatment status (see *section 4.4*).

Re-treatment, after liver function tests return to that of the patient's baseline, may be given at a reduced dose of 500 mg once daily. For patients being re-treated, serum transaminases and bilirubin should be monitored at a minimum of every 2 weeks for the first 3 months and monthly thereafter. If hepatotoxicity recurs at the reduced dose of 500 mg daily, treatment should be discontinued. Reduced doses should not be taken with food (see posology).

If patients develop severe hepatotoxicity (ALT or AST 20 times the ULN) anytime while on therapy, **ENORTERIB** should be discontinued and patients should not be re-treated with **ENORTERIB**.

Renal impairment:

No dose adjustment is necessary for patients with renal impairment (see *section 5.2*).

Paediatric population:

There is no relevant use of **ENORTERIB** in paediatric patients, as prostate cancer is not present in the paediatric population.

Method of administration:

ENORTERIB is administered by the oral route (tablets).

ENORTERIB should be taken on an empty stomach, at least 1 hour before or at least 2 hours after a meal. The tablets should be swallowed whole with water.

For precautions to be taken before handling or administering **ENORTERIB** (see *section 6.6*).

Based on its mechanism of action, **ENORTERIB** may harm a developing foetus, therefore women (including healthcare professionals), who are pregnant or women who may be pregnant, should not handle **ENORTERIB** without protection e.g., gloves (see *sections 4.6* and *6.6*).

4.3 Contraindications

ENORTERIB is contraindicated in:

- Patients with hypersensitivity to the active substance (abiraterone) or any of the excipients listed in section 6.1.
- Women who are or may be potentially pregnant (see *section 4.6*)
- Moderate to severe hepatic impairment (Child-Pugh class B and C) (see *sections 4.2*, *4.4* and *5.2*)
- Pregnancy and lactation (see *section 4.6*)
- Women should not use **ENORTERIB**
- Women who are pregnant, planning to become pregnant or women of childbearing age (see *section 4.6*)
- Concomitant administration with rifampicin (see *section 4.5*)
- Concomitant administration with prednisone/ prednisolone and Ra-223

4.4 Special warnings and precautions for use

Hypertension, hypokalaemia and fluid retention due to mineralocorticoid excess:

ENORTERIB may cause hypertension, hypokalaemia and fluid retention (see *section 4.8*) as a consequence of increased mineralocorticoid levels resulting from 17α-hydroxylase/C17,20-lyase (CYP17) inhibition (see *section 5.2*). Co-administration of a corticosteroid suppresses adrenocorticotropic hormone (ACTH) drive, resulting in a reduction in incidence and severity of these adverse reactions. Caution is required in treating patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalaemia (e.g. those on cardiac glycosides) or fluid retention e.g., those with heart failure, severe or unstable angina pectoris, recent myocardial infarction or ventricular dysrhythmia and those with severe renal impairment.

ENORTERIB should be used with caution in patients with a history of cardiovascular disease. The safety of **ENORTERIB** in patients with left ventricular ejection fraction < 50 % or the New York Heart Association (NYHA) Class III or IV heart failure, has not been established. Before treatment with **ENORTERIB**, hypertension must be controlled and hypokalaemia must be corrected. Blood pressure, serum potassium and fluid retention should be monitored at least monthly.

Before treating patients with a significant risk for congestive heart failure (e.g., a history of cardiac failure, uncontrolled hypertension, or cardiac events such as ischaemic heart disease), an assessment of cardiac function (e.g., echocardiogram) must be considered. Prior to treatment with **ENORTERIB** cardiac failure should be treated and cardiac function be optimised. Hypertension, hypokalaemia and fluid retention should be corrected and controlled. During treatment blood pressure, serum potassium and fluid retention (weight gain, peripheral oedema), and other signs and symptoms of congestive heart failure should be monitored every 2 weeks for 3 months, then monthly thereafter and abnormalities corrected. QT prolongation has been observed in patients experiencing hypokalaemia in association with abiraterone treatment. Assess cardiac function as clinically indicated, institute appropriate management and consider discontinuation of this treatment if there is a clinically significant decrease in cardiac function (see *section 4.2*).

Hepatotoxicity and hepatic impairment:

Marked increases in liver enzymes leading to **ENORTERIB** discontinuation or dose modification have occurred (see *section 4.8*). Serum transaminase and bilirubin levels should be measured prior to starting treatment with **ENORTERIB**, every 2 weeks for the first 3 months of treatment, and monthly thereafter. If clinical symptoms or signs suggestive of hepatotoxicity develop, serum transaminases, should be measured immediately. If at any time the ALT or AST rises above five times the upper limit of normal (ULN) or the bilirubin rises above three times ULN, treatment with **ENORTERIB** should be interrupted immediately and liver function closely monitored.

Re-treatment with **ENORTERIB** may take place only after return of liver function tests to the patient's baseline and at a reduced dose (see *section 4.2*).

If patients develop severe hepatotoxicity (ALT/ AST 20 times the upper limit of normal) at any time while on therapy, **ENORTERIB** should be discontinued and patients should not be re-treated with **ENORTERIB**.

There are no data on the clinical safety and efficacy of multiple doses of **ENORTERIB** when administered to patients with moderate or severe hepatic impairment (Child Pugh Class B or C). **ENORTERIB** should not be used in patients with moderate to severe hepatic impairment (see *section 4.2, 4.3* and *5.2*).

There have been post-marketing reports of acute liver failure and fulminant hepatitis, some with fatal outcome (see *section 4.8*).

Testosterone deficiency is associated with higher serum and hepatic levels of triglycerides and higher serum levels of low-density lipoprotein (LDL) in the body, with significant increases in fasting plasma glucose and insulin levels. Patients who receive androgen deprivation therapy (ADT) are at greater risk of being diagnosed with non-alcoholic fatty liver disease (NAFLD) and to show significant increase and/or incidences of liver disease. As abiraterone (as contained in **ENORTERIB**) is commonly used in conjunction with ADT (see section 4.1), the same can be expected.

Corticosteroid withdrawal and coverage of stress situations:

Caution is advised and monitoring for symptoms and signs of adrenocortical insufficiency should occur, particularly if patients are withdrawn from prednisone or prednisolone. If **ENORTERIB** is continued after corticosteroids are withdrawn, patients should be monitored for symptoms of mineralocorticoid excess.

In patients on prednisone or prednisolone who are subjected to unusual stress, increased dosage of corticosteroids may be indicated before, during and after the stressful situation.

Bone density:

Decreased bone density may occur in men with metastatic advanced prostate cancer. The use of **ENORTERIB** in combination with a glucocorticoid could increase this effect.

Use with chemotherapy:

The safety and efficacy of concomitant use of **ENORTERIB** with cytotoxic chemotherapy has not been established (see *section 5.1*).

Combination of abiraterone and prednisone/ prednisolone with Ra-223:

Treatment with abiraterone and prednisone/ prednisolone in combination with Ra-223 is contraindicated (see *section 4.3*) due to an increased risk of fractures and a trend for increased mortality.

It is recommended that subsequent treatment with Ra-223 is not initiated for at least 5 days after the last administration of **ENORTERIB** in combination with prednisone/ prednisolone.

Hypoglycaemia

Cases of hypoglycaemia have been reported with **ENORTERIB** plus prednisone/ prednisolone was administered to patients with pre-existing diabetes receiving pioglitazone or repaglinide. Blood glucose should be monitored in patients with diabetes.

Hyperglycaemia:

The use of glucocorticoids could increase hyperglycaemia, therefore blood sugar should be measured frequently in patients with diabetes.

Vaccination with live attenuated bacterial or viral vaccines:

Prostate cancer patients on treatment should receive guidance on age and indication appropriate vaccinations, in particular live attenuated bacterial or viral vaccines. Patients should also be advised to take extra precaution should they come into contact with someone who has received a live vaccine.

Tuberculosis and/ or HIV:

Prostate cancer patients with tuberculosis and/ or HIV, who are not well-controlled on treatment should be monitored closely.

Prior use of ketoconazole:

Lower rates of response might be expected in patients previously treated with ketoconazole for prostate cancer.

Potential risks:

Anaemia and sexual dysfunction may occur in men with metastatic prostate cancer including those undergoing treatment with **ENORTERIB**.

Skeletal muscle effects:

Cases of myopathy and rhabdomyolysis have been reported in patients treated with **ENORTERIB**. Most cases developed within the first 6 months of treatment and recovered after **ENORTERIB** withdrawal. Caution is recommended in patients concomitantly treated with medicinal products known to be associated with myopathy/rhabdomyolysis.

Interactions with other medicinal products:

Strong inducers of CYP3A4 during treatment are to be avoided unless there is no therapeutic alternative, due to risk of decreased exposure to abiraterone (see *section 4.5*).

Excipient warnings:

ENORTERIB contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **ENORTERIB**.

4.5 Interaction with other medicines and other forms of interaction

Effect of food on abiraterone acetate

Administration of **ENORTERIB** with food significantly increases the absorption of abiraterone acetate. The efficacy and safety of **ENORTERIB** given with food have not been established. **ENORTERIB must not be taken with food** (see *sections 4.2* and *5.2*).

Interactions with other medicinal products

Potential for other medicinal products to affect abiraterone exposures

In a clinical pharmacokinetic interaction study of healthy subjects pretreated with a strong CYP3A4 inducer rifampicin, 600 mg daily for 6 days followed by a single dose of abiraterone acetate 1000 mg, the mean plasma AUC_{∞} of abiraterone was decreased by 55 %.

Other strong inducers of CYP3A4 (e.g., phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital, St John's wort [Hypericum perforatum]) during treatment with **ENORTERIB** are to be avoided.

Co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone as in **ENORTERIB**.

Potential to affect exposures to other medicinal products

Abiraterone as in **ENORTERIB** is an inhibitor of the hepatic drug-metabolising enzymes CYP2D6 and CYP2C8.

In a study to determine the effects of abiraterone acetate (plus prednisone) on a single dose of the CYP2D6 substrate dextromethorphan, the systemic exposure (AUC) of dextromethorphan was

increased approximately 2,9-fold. The AUC_{24} for dextrorphan, the active metabolite of dextromethorphan, increased approximately 33 %.

Caution is advised when administering **ENORTERIB** with medicinal products activated by or metabolised by CYP2D6, particularly with medicinal products that have a narrow therapeutic index. Dose reduction of medicinal products with a narrow therapeutic index that are metabolised by CYP2D6 should be considered. Examples of medicinal products metabolised by CYP2D6 include metoprolol, propranolol, desipramine, venlafaxine, haloperidol, risperidone, propafenone, flecainide, codeine, oxycodone and tramadol (the latter three medicinal products requiring CYP2D6 to form their active analgesic metabolites).

In a CYP2C8 interaction trial in healthy subjects, the AUC of pioglitazone was increased by 46 % and the AUCs for M-III and M-IV, the active metabolites of pioglitazone, each decreased by 10 % when pioglitazone was given together with a single dose of 1000 mg abiraterone acetate. When **ENORTERIB** is combined with medicinal products that are predominantly eliminated by CYP2C8, patients should be monitored for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly.

In vitro, the major metabolites abiraterone sulphate and N-oxide abiraterone sulphate were shown to inhibit the hepatic uptake transporter OATP1B1 and as a consequence it may increase the concentrations of medicinal products eliminated by OATP1B1. There are no clinical data available to confirm transporter-based interaction.

Use with products known to prolong QT interval

Since androgen deprivation treatment may prolong the QT interval, caution is advised when administering **ENORTERIB** with medicinal products known to prolong the QT interval or medicinal products able to induce torsades de pointes such as class IA (e.g., quinidine, disopyramide) or class

III (e.g., amiodarone, sotalol, dofetilide, ibutilide) antidysrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc.

Use with Spironolactone

Spironolactone binds to the androgen receptor and may increase prostate specific antigen (PSA) levels. Use with **ENORTERIB** is not recommended (see *section 5.1*).

Concomitant use with eplenerone

There is no clinical study data related to concomitant use of eplenerone with **ENORTERIB**.

4.6 Fertility, pregnancy and lactation

Women should not use **ENORTERIB**.

Women of childbearing potential

There are no human data on the use of **ENORTERIB** in pregnancy. **ENORTERIB** is not for use in women of childbearing potential. Maternal use of a CYP17 inhibitor is expected to produce changes in hormone levels that could affect development of the foetus.

Contraception in males and females

Studies in animals have shown reproductive toxicity.

It is not known whether abiraterone or its metabolites are present in semen, therefore a condom is required if the patient is engaged in sexual activity with a pregnant woman. If the patient is engaged in sex with a woman of childbearing potential, a condom is required along with another effective contraceptive method until one week after the last dose of **ENORTERIB**.

Pregnancy:

ENORTERIB is contraindicated in women who are or may potentially be pregnant (see *section 4.3*).

Pregnant women or women of child-bearing potential should handle **ENORTERIB** with gloves (see *section 6.6*).

Breastfeeding:

ENORTERIB is not for use in women. It is not known whether abiraterone acetate or its metabolites are excreted in human breast milk.

Fertility:

In fertility studies in both male and female rats, abiraterone acetate reduced fertility, which was completely reversible in 4 to 16 weeks after abiraterone acetate as in **ENORTERIB** was stopped.
It is recommended to store semen before starting treatment with **ENORTERIB** in patients who might want to father a child.

4.7 Effects on ability to drive and use machines

ENORTERIB has no or negligible influence on the ability to drive or use machines. Patients should not drive and use machines before they know how treatment with **ENORTERIB** affects their ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequent undesirable effects occurring with **ENORTERIB** use, are peripheral oedema, hypokalaemia, hypertension and urinary tract infection, and increased alanine aminotransferase and/ or increased aspartate aminotransferase. **ENORTERIB** may cause hypertension, hypokalaemia and fluid retention as a pharmacodynamic consequence of its mechanism of action. Other important adverse reactions include cardiac disorders, hepatotoxicity, fractures and allergic alveolitis.

b. Tabulated summary of adverse reactions

System Organ Class	Adverse Reactions	Frequency Category
Infections and infestations	Urinary tract infection, sepsis	Frequent
Immune system disorders	Anaphylactic reaction	Frequency unknown
Endocrine disorders	Adrenal insufficiency	Less frequent
Metabolism and nutrition disorders	Hypokalaemia, hypertriglyceridemia	Frequent
Cardiac disorders	Cardiac failure (including congestive heart failure, left ventricular dysfunction and decreased left ventricular ejection fraction), angina pectoris, cardiac dysrhythmias, arterial fibrillation, tachycardia	Frequent
	Myocardial infarction, QT prolongation	Frequency unknown
Vascular disorders	Hypertension	Frequent
Respiratory, thoracic and mediastinal disorders	Allergic alveolitis	Less frequent
Gastrointestinal disorders	Diarrhoea, dyspepsia	Frequent

Hepatobiliary disorders	Hepatotoxicity, abnormal hepatic functions including elevated hepatic function tests such as ALT, AST and total bilirubin	Frequent
	hepatitis fulminant, acute hepatic failure	Less frequent
Skin and subcutaneous tissue disorders	Rash	Frequent
Musculoskeletal and connective tissue disorders	Myopathy, rhabdomyolysis	Less frequent
Renal and urinary disorders	Haematuria	Frequent
General disorders and administration site disorders	Peripheral oedema	Frequent
Injury, poisoning and procedural complications	Fractures includes osteoporosis and all fractures with the exception of pathological fractures	Frequent

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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

In overdose side effects can be precipitated and/or be of increased severity (see *section 4.8*). There is no specific antidote. In the event of an overdose, administration of **ENORTERIB** should be discontinued. Treatment is symptomatic and supportive, including monitoring of cardiac and hepatic function, serum potassium and blood pressure. Liver function also needs to be assessed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.21.12 Hormone inhibitors

Mechanism of action

Abiraterone acetate is converted *in vivo* to abiraterone, an androgen biosynthesis inhibitor. Specifically, abiraterone selectively inhibits the enzyme 17α-hydroxylase/ C17,20-lyase (CYP17). This enzyme is expressed in and is required for androgen biosynthesis in testicular, adrenal and prostatic tumour tissues.

CYP17 catalyses the conversion of pregnenolone and progesterone into testosterone precursors, DHEA and androstenedione, respectively by 17α-hydroxylation and cleavage of the C17,20 bond. CYP17 inhibition also results in increased mineralocorticoid production by the adrenals (see *section 4.4*).

Androgen sensitive prostatic carcinoma responds to treatment that decreases androgen levels. Androgen deprivation therapies, such as treatment with LNRH agonists or orchiectomy, decrease androgen production in the testes but do not affect androgen production by the adrenals or in the

tumour. Treatment with abiraterone acetate decreases serum testosterone to undetectable levels (using commercial assays) when given with LNRH agonists (or orchiectomy).

Pharmacodynamic effects:

Abiraterone acetate decreases serum testosterone and other androgens to levels lower than those achieved by the use of LHRH agonists alone or orchiectomy. This results from the selective inhibition of the CYP17 enzyme required for androgen biosynthesis. Prostate specific antigen (PSA) serves as a biomarker in patients with prostate cancer. In a phase 3 clinical study of patients who failed prior chemotherapy with taxanes, 38 % of patients treated with abiraterone acetate, versus 10 % of patients treated with placebo, had at least a 50 % decline from baseline in PSA levels.

5.2 Pharmacokinetic properties

Following administration of abiraterone acetate, the pharmacokinetics of abiraterone and abiraterone acetate have been studied in healthy subjects, patients with metastatic advanced prostate cancer and subjects without cancer with hepatic or renal impairment. Abiraterone acetate is rapidly converted *in vivo* to abiraterone, an androgen biosynthesis inhibitor (see *section 5.2*).

Absorption:

Following oral administration of abiraterone acetate in the fasting state, the median time to reach maximum plasma abiraterone concentration is approximately 2 hours.

Administration of abiraterone acetate with food, compared with administration in a fasted state, results in up to 10-fold (AUC) and 17-fold (C_{max}) increase in mean systemic exposure of abiraterone, depending on the fat content of the meal. Given the normal variation in the content and composition of meals, taking abiraterone acetate with meals has the potential to result in highly variable exposures.

Therefore, **abiraterone acetate must not be taken with food**.

Abiraterone acetate should be taken at least two hours after eating and no food should be eaten for at least one hour after taking **ENORTERIB**. The tablets should be swallowed whole with water (see *section 4.2*).

Distribution:

The plasma protein binding of ^{14}C-abiraterone in human plasma is 99,8 %. The apparent volume of distribution is approximately 5630 ℓ, suggesting that abiraterone extensively distributes to peripheral tissues.

Biotransformation:

Following oral administration of ^{14}C-abiraterone acetate as capsules, abiraterone acetate is hydrolysed to abiraterone, which then undergoes metabolism including sulphation, hydroxylation and oxidation primarily in the liver. The majority of circulating radioactivity (approximately 92 %) is found in the form of metabolites of abiraterone. Of 15 detectable metabolites, 2 main metabolites, abiraterone sulphate and N-oxide abiraterone sulphate, each represents approximately 43 % of total radioactivity.

Elimination:

The mean half-life of abiraterone in plasma is approximately 15 hours based on data from healthy subjects. Following oral administration of ^{14}C-abiraterone acetate 1 g, approximately 88 % of the radioactive dose is recovered in faeces and approximately 5 % in urine. The major compounds present in faeces are unchanged abiraterone acetate and abiraterone (approximately 55 % and 22 % of the administered dose, respectively).

Patients with hepatic impairment:

The pharmacokinetics of abiraterone was examined in subjects with pre-existing mild or moderate hepatic impairment (Child-Pugh Class A and B, respectively) and in healthy control subjects. Systemic exposure to abiraterone after a single oral 1 g dose increased by approximately 11 % and

260 % in subjects with mild and moderate pre-existing hepatic impairment, respectively. The mean half-life of abiraterone is prolonged to approximately 18 hours in subjects with mild hepatic impairment and to

approximately 19 hours in subjects with moderate hepatic impairment. No dose adjustment is necessary for patients with pre-existing mild hepatic impairment.

There are no data on the clinical safety and efficacy of multiple doses of abiraterone when administered to patients with moderate or severe hepatic impairment (Child Pugh Class B or C). No dose adjustment can be predicted.

Abiraterone acetate should not be used in patients with moderate to severe hepatic impairment.

For patients who develop hepatotoxicity during treatment with abiraterone acetate, suspension of treatment and dose adjustment may be required (see *section 4.2* and *4.4*).

Patients with renal impairment:

The pharmacokinetics of abiraterone acetate was compared in patients with end-stage renal disease on a stable haemodialysis schedule versus matched control subjects with normal renal function. Systemic exposure to abiraterone after a single oral 1 g dose did not increase in subjects with end stage renal disease on dialysis. Administration of abiraterone acetate in patients with renal impairment, including severe renal impairment, does not require dose reduction (see *section 4.2*).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate, sodium lauryl sulphate, magnesium stearate, microcrystalline cellulose, povidone K-30, Opadry II 85F500121.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30 °C.

Keep tightly closed.

Protect from light.

KEEP OUT OF THE REACH OF CHILDREN.

6.5 Nature and contents of container

60 Tablets packed in 150 mL HDPE container with CR closure 38 mm with liner.

6.6 Special precautions for disposal and other handling

Based on its mechanism of action **ENORTERIB** may harm a developing foetus. Caution should be exercised when handling and administering **ENORTERIB** tablets. Women (including healthcare workers) who are pregnant or women who may be pregnant, should not handle **ENORTERIB** tablets without protection e.g., gloves (see *section 4.6*).

Any unused medicine should be returned to the pharmacy to be correctly disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Glenmark Pharmaceuticals South Africa (Pty) Ltd

34 Monte Carlo Crescent,

Block A, First floor,

Kyalami Park,

Midrand,

1684

8. REGISTRATION NUMBER(S)

57/21.12/0051

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

To be allocated

10. DATE OF REVISION OF TEXT

30 June 2026