1.3.1.1 PROFESSIONAL INFORMATION (CURRENT APPROVED)

SCHEDULING STATUS: **S 4**

PROPRIETARY NAME (and Dosage Form):

Nexiam® 20 mg; Nexiam® 40 mg (Gastric-Resistant Tablet)

Nexiam® 10 mg Sachets (Granules)

COMPOSITION:

NEXIAM 20 mg:

Each gastric-resistant tablet contains esomeprazole magnesium trihydrate 22,3 mg (equivalent to esomeprazole 20 mg) in the form of a multiple unit pellet system (MUPS).

NEXIAM 40 mg:

Each gastric-resistant tablet contains esomeprazole magnesium trihydrate 44,5 mg (equivalent to esomeprazole 40 mg) in the form of a multiple unit pellet system (MUPS).

List of excipients for NEXIAM 20 & 40 mg tablets:

Crospovidone, glycerol monostearate, hypromellose, hydroxypropylcellulose, iron oxide, magnesium stearate, methacrylic acid-ethyl acrylate copolymer, microcrystalline cellulose, macrogol, polysorbate 80, synthetic paraffin, sugar spheres (sucrose and maize starch), sodium stearyl fumarate, talc, triethyl citrate, titanium dioxide.

NEXIAM 10 mg Sachets:

Each sachet contains esomeprazole magnesium trihydrate 11,1 mg
(equivalent to esomeprazole 10 mg) in the form of gastro-resistant granules for oral suspension.

List of excipients for NEXIAM 10 mg sachets:

Glycerol monostearate, hyprolose, hypromellose, magnesium stearate, methacrylic acid copolymer, polysorbate 80, sugar spheres, talc, triethyl citrate, dextrose, xanthan gum, crospovidone, citric acid, iron oxide (yellow) (E 172).

Contains sugar (sucrose).

PHARMACOLOGICAL CLASSIFICATION:

A 11.4.3 Medicines acting on gastro-intestinal tract. Other.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Esomeprazole, the S-isomer of omeprazole, reduces gastric acid secretion through specific inhibition of the acid pump in the parietal cell, where it is concentrated and converted to the active form in the acidic environment of the secretory canaliculi and inhibits the enzyme H^+K^+-ATPase – the acid pump. This effect on the final step of the gastric acid secretion is dose-dependent and provides for effective inhibition of both basal and stimulated acid secretion.

Effect on gastric acid secretion:

After oral dosing with esomeprazole 20 mg and 40 mg, the onset of effect occurs within 1 hour. After repeated administration with 20 mg esomeprazole once daily for 5 days, mean peak acid output after pentagastrin stimulation is decreased by 90 % when measured 6-7 hours after dosing on day 5.

After 5 days of oral dosing with 20 mg and 40 mg of esomeprazole, intragastric pH above 4 was maintained for a mean time of 13 hours and 17 hours, respectively over 24 hours in symptomatic Gastro-oesophageal Reflux Disease (GORD) patients. The proportion of patients maintaining an intragastric pH above 4 for at least 8, 12 and 16 hours were 76 %, 54 % and 24 % respectively for esomeprazole 20 mg. Corresponding proportions for esomeprazole 40 mg were 97 %, 92 % and 56 % respectively.

Using AUC as a surrogate parameter for plasma concentration, a relationship between inhibition of acid secretion and exposure has been shown.

Food intake had no significant influence on the effect of esomeprazole on intragastric acidity.

Other effects related to acid inhibition:

During long-term treatment with antisecretory medicines, gastric glandular cysts occur. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

Pharmacokinetic properties:

Absorption and distribution:

Esomeprazole is acid labile and is administered orally as enteric-coated granules. *In vivo* conversion to the R-isomer is negligible. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 89 % after repeated once-daily administration. The apparent volume of distribution at steady state in healthy subjects is approximately 0,22 litres/kg body weight. Esomeprazole is 97 % plasma protein bound.

Metabolism and excretion:

Esomeprazole is completely metabolised by the cytochrome P450 system (CYP). The major part of the metabolism of esomeprazole is dependent on the polymorphic CYP2C19, responsible for the formation of the hydroxy- and desmethyl metabolites of esomeprazole. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of esomeprazole sulphone, the main metabolite in plasma.

The parameters below reflect mainly the pharmacokinetics in individuals with a functional CYP2C19 enzyme (extensive metabolisers).

Total plasma clearance is about 17 litres per hour after a single dose and about 9 litres per hour after repeated administration. The plasma elimination half-life is about 1,3 hours after repeated once-daily dosing. The area under the plasma concentration-time curve increases with repeated administration of esomeprazole. This increase is dose-dependent and results in a non-linear dose-AUC relationship after repeated administration. This time- and dose-dependency is due to a decrease of first pass metabolism and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by esomeprazole and/or its sulphone metabolite. Esomeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration.

The major metabolites of esomeprazole have no effect on gastric acid secretion. Almost 80 % of an oral dose of esomeprazole is excreted as metabolites in the urine, the remainder in the faeces. Less than 1 % of the parent compound is found in urine.

Special patient populations:

Approximately 1-2 % of the population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 40 mg esomeprazole, the mean area under the plasma concentration-time curve was approximately 100 % higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60 %.

The metabolism of esomeprazole is not significantly changed in elderly subjects (71-80 years of age).

Following a single dose of 40 mg esomeprazole the mean area under the plasma concentration-time curve is approximately 30 % higher in females than in males. No gender difference is seen after repeated once-daily administration. These findings have no implications for the dosage of esomeprazole.

The metabolism of esomeprazole in patients with mild to moderate liver dysfunction may be impaired. The metabolic rate is decreased in patients with severe liver dysfunction resulting in a doubling of the area under the plasma concentration-time curve of esomeprazole. Therefore, a maximum of 20 mg should not be exceeded in patients with severe dysfunction. Esomeprazole or its major metabolites do not show any tendency to accumulate with once-daily dosing.

No studies have been performed in patients with decreased renal function. Since the kidney is responsible for the excretion of the metabolites of esomeprazole, but not for the

elimination of the parent compound, the metabolism of esomeprazole is not expected to be changed in patients with impaired renal function.

Following repeated dose administration of 20 mg and 40 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma concentration (t_{max}) in 12-18 year-olds was similar to that in adults for both esomeprazole doses.

Following repeated dose administration of 10 mg and 20 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma concentration (t_{max}) for the 10 mg dose was similar across the 1-11 year-olds and similar to the total exposure seen with the 20 mg dose in 12-18 year-olds and adults. The 20 mg dose resulted in higher exposure in 6-11 year-olds compared to 12-18 year-olds and adults.

Repeated dose administration of 5 mg esomeprazole resulted in insufficient exposure in 1-5 year-olds.

INDICATIONS:

NEXIAM 20 and 40 mg tablets and NEXIAM 10 mg Sachets are indicated for:

Gastro-oesophageal Reflux Disease (GORD):

- treatment of erosive reflux oesophagitis
- long-term management of patients with healed oesophagitis to prevent relapse
- symptomatic treatment of Gastro-oesophageal Reflux Disease (GORD).

Patients requiring continued NSAID therapy:

- prevention of gastric and duodenal ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy in patients at risk.

In combination with appropriate antibacterial therapeutic regimen for the eradication of Helicobacter pylori:

- healing of *Helicobacter pylori* associated duodenal ulcer and
- prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcer disease.

NEXIAM has been used in pathological hypersecretory conditions including Zollinger-Ellison syndrome and idiopathic hypersecretion.

CONTRAINDICATIONS:

Known hypersensitivity to NEXIAM, substituted benzimidazoles or any other constituents of the formulation.

Concomitant administration of NEXIAM with atazanavir or nelfinavir (see "INTERACTIONS").

WARNINGS AND SPECIAL PRECAUTIONS:

NEXIAM is not indicated for mild gastrointestinal complaints such as nervous dyspepsia.

Prior to treatment or in the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melaena) and when gastric ulcer is suspected or present, the possibility of malignancy of gastric ulcer or a malignant disease of the oesophagus should be excluded, as the treatment with NEXIAM may alleviate the symptoms of malignant ulcers and can thus delay diagnosis.

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.

Concommitant administration of clopidogrel and esomeprazole resulted in decreased exposure to the active metabolite of clopidogrel by an average of 40 %. The maximum inhibition of (ADP induced) platelet aggregation decreased by an average of 14 %. Based on these data, concomitant use of NEXIAM and clopidogrel should be avoided.

During treatment with antisecretory medicines, serum gastrin increases in response to the decreased acid secretion. Also chromogranin A (CgA) increase due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours. To avoid this interference, the esomeprazole treatment should be temporarily stopped 5 days before CgA measurements.

Decreased gastric acidity increases gastric contents counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors may lead to increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and, in hospitalised patients, possibly also *Clostridium difficile*.

Clostridium difficile is a bacterium that can cause severe debilitating diarrhoea that does not improve. Symptoms may include watery stools, abdominal pain, fever, and patients may develop more serious intestinal conditions.

Special Precautions:

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.

Decreased gastric acidity due to any means including proton pump inhibitors such as NEXIAM tablets, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with NEXIAM may lead to increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and also *Clostridium difficile* in hospitalised patients.

NEXIAM contains sucrose and is not suitable for patients with glucose-galactose malabsorption syndrome, fructose intolerance, or sucrose isomaltase deficiency.

Effects on the ability to drive and use machines:

NEXIAM may cause dizziness and blurred vision, thereby affecting the ability to drive or use machinery.

INTERACTIONS:

Effects of NEXIAM on the pharmacokinetics of other medicines:

The gastric acid suppression during treatment with NEXIAM, might decrease or increase the absorption of medicines with a gastric pH dependent absorption. The absorption of medicines such as ketoconazole, itraconazole and erlotinib can decrease while the absorption of medicines such as digoxin can increase during treatment with NEXIAM. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10 % (up to 30 % in 2 out of 10 subjects). Digoxin toxicity has been reported. Caution should be exercised when NEXIAM is given at high doses in elderly patients. Therapeutic monitoring of digoxin levels should be done.

NEXIAM inhibits CYP2C19, the major NEXIAM metabolising enzyme. Concomitant administration of 30 mg NEXIAM resulted in a 45 % decrease in clearance of the CYP2C19 substrate diazepam. This interaction is unlikely to be of clinical relevance. Concomitant administration of 40 mg NEXIAM resulted in a 13 % increase in trough plasma levels of phenytoin in epileptic patients; dose adjustment was not required in this study.

Concomitant administration of 40 mg NEXIAM to warfarin-treated patients showed that, despite elevation in the trough plasma concentration of the less potent R-isomer of warfarin, the coagulation times were within the accepted range.

From post marketed use, cases of elevated INR of clinical significance have been reported during concomitant treatment with warfarin. Close monitoring is recommended when warfarin is co-administered with NEXIAM at initiation of treatment, during the treatment and at ending treatment.

Results from studies in healthy subjects have shown a pharmacokinetic/ pharmacodynamic interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40 mg p.o. daily) resulting in decreased exposure to the active metabolite of clopidogrel by an average of 40 % and resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14 %.

Based on these data, concomitant use of NEXIAM and clopidogrel should be avoided.

Omeprazole as well as esomeprazole act as inhibitors of CYP 2C19. Omeprazole given in doses of 40 mg to healthy subjects in a cross-over study, increased C_{max} and AUC for

cilostazol by 18 % and 26 % respectively, and one of its metabolites by 29 % and 69 % respectively.
NEXIAM can be suspected to have a similar effect.

In healthy volunteers, concomitant administration of 40 mg NEXIAM resulted in a 32 % increase in area under the plasma concentration-time curve (AUC) and a 31 % prolongation of elimination half-life ($t_{½}$) but no significant increase in peak plasma levels of cisapride. This interaction did not alter the influence of cisapride on cardiac electrophysiology.

When given together with proton pump inhibitors, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of NEXIAM may need to be considered.

NEXIAM has been shown to have no clinically relevant effects on the pharmacokinetics of amoxicillin or quinidine.

Studies evaluating concomitant administration of NEXIAM and either naproxen (non-selective NSAID) or rofecoxib (COX-2-selective NSAID) did not identify any clinically relevant interaction.

Concomitant administration of NEXIAM may significantly reduce the plasma levels of atazanavir.

Omeprazole has been reported to interact with some antiretroviral medicines. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral medicines. Other possible interaction mechanisms are via CYP2C19. For some antiretroviral medicines, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not

recommended. For other antiretroviral medicines, such as saquinavir, increased serum levels have been reported of 80-100 %. There are also some antiretroviral medicines for which unchanged serum levels have been reported when given with omeprazole. Close monitoring or dose alteration is recommended.

Concomitant administration with esomeprazole and antiretroviral medicines such as atazanavir and nelfinavir is not recommended. NEXIAM substantially decreases the concentration of atazanavir and nelfinavir (see *"*CONTRAINDICATIONS*"*).

Co-administration of esomeprazole (40 mg once daily) reduced mean nelfinavir exposure by approximately 40 % and the mean exposure of the pharmacological active metabolite was reduced by approximately 75-90 %.

Tipranavir may decrease the concentration of NEXIAM. Co-administration is not recommended. However, if used concurrently, the dose of NEXIAM should be increased.

Effects of other medicines on the pharmacokinetics of NEXIAM:
NEXIAM is metabolised by CYP2C19 and CYP3A4. Concomitant administration of NEXIAM and a CYP3A4 inhibitor, clarithromycin (500 mg b.i.d.), resulted in a doubling of the exposure (AUC) to NEXIAM.
Concomitant administration of NEXIAM and a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than tripling of the NEXIAM exposure. Dose adjustment of NEXIAM is not required.

Medicines known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St. John's Wort) may lead to decreased esomeprazole serum levels by increasing the esomeprazole metabolism.

PREGNANCY AND LACTATION:

Safety during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

NEXIAM 20 and 40 mg tablets:

The tablets should be swallowed whole with liquid. The tablets should not be chewed or crushed.

The tablets can also be dispersed in half a glass of non-carbonated water. No other liquids should be used. Stir until the tablets disintegrate and drink the liquid with the pellets immediately or within 30 minutes. Rinse the glass with half a glass of water and drink. The pellets must not be chewed or crushed. For patients who cannot swallow, the tablets can be dispersed in non-carbonated water and administered through a gastric tube.

NEXIAM 10 mg Sachets:

The contents of a 10 mg sachet should be emptied into a container containing a tablespoon (15 ml) of water. Stir the contents and leave for a few minutes to thicken. Stir again and drink within 30 minutes. If any material remains after drinking, add more water, stir, and drink immediately.

For patients who have a nasogastric or gastric tube in place, the contents of the sachet can be added to a syringe containing 15 ml of water. Immediately shake the syringe and leave

for a few minutes to thicken. Shake the syringe and inject through the nasogastric or gastric tube within 30 minutes. Refill the syringe with an equal amount of water and shake and flush any remaining contents from the nasogastric or gastric tube into the stomach.

Gastro-oesophageal Reflux Disease (GORD):

- treatment of erosive reflux oesophagitis

  40 mg once daily for 4 weeks

  An additional 4 weeks treatment is recommended for patients in whom oesophagitis has not healed or who have persistent symptoms.

- long-term management of patients with healed oesophagitis to prevent relapse

  20 mg once daily.

- symptomatic treatment of Gastro-oesophageal Reflux Disease (GORD)

  20 mg once daily in patients without oesophagitis. If symptom control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using an on demand regimen, taking 20 mg once daily, when needed.

Patients requiring continued NSAID therapy:

- prevention of gastric and duodenal ulcers associated with NSAID therapy in patients at risk

  20 mg or 40 mg once daily.

In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori and

- healing of *Helicobacter pylori* associated duodenal ulcer and prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcer disease

  20 mg NEXIAM with 1 g amoxicillin and 500 mg clarithromycin, all twice daily for 7 days.

Pathological hypersecretory conditions including Zollinger-Ellison syndrome and idiopathic hypersecretion:

The recommended initial dosage is NEXIAM 40 mg twice daily. The dosage should then be individually adjusted and treatment continued as long as clinically indicated. Doses up to 120 mg twice daily have been administered.

Adolescents 12-18 years:

Gastro-oesophageal Reflux Disease (GORD):

- treatment of erosive reflux oesophagitis

  40 mg once daily for 4 weeks

  An additional 4 weeks treatment is recommended for patients in whom oesophagitis has not healed or who have persistent symptoms.

- long-term management of patients with healed oesophagitis to prevent relapse

  20 mg once daily.

- Symptomatic treatment of Gastro-oesophageal Reflux Disease (GORD)

  20 mg once daily in patients without oesophagitis. If symptom control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using 20 mg once daily under medical supervision.

Children 1-11 years:

Gastro-oesophageal Reflux Disease (GORD):

- treatment of erosive reflux oesophagitis

  Weight < 20 kg: 10 mg once daily for 8 weeks.

  Weight ≥ 20 kg: 10 mg or 20 mg once daily for 8 weeks.

- symptomatic treatment of Gastro-oesophageal Reflux Disease (GORD)

  10 mg once daily for up to 8 weeks.

- long-term management of patients with healed oesophagitis to prevent relapse

  10 mg once daily.

Doses over 1 mg/kg/day have not been studied.

Children:

NEXIAM should not be used in children younger than 1 year since no data is available.

Impaired renal function:

Dose adjustment is not required in patients with impaired renal function. Due to limited experience in patients with severe renal insufficiency, such patients should be treated with caution.

Impaired hepatic function:

Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a maximum daily dose of 20 mg NEXIAM should be used.

Elderly:

Dose adjustment is not required in the elderly.

SIDE EFFECTS:

The following definitions of frequency are used:

Common:	≥ 1/100
Uncommon:	≥ 1/1 000 and < 1/100
Rare:	≥ 1/10 000 and < 1/1 000
Very rare:	< 1/10 000

Clinical trials:

The following adverse reactions have been identified or suspected in the clinical trials programme for NEXIAM. None, however, were found to be dose-related.

Blood and lymphatic system disorders:

Rare:	Leukopenia, thrombocytopenia

Immune system disorders:

Rare:	Hypersensitivity reactions e.g. angioedema and anaphylactic reaction/shock

Metabolism and nutrition disorders:

Uncommon: Peripheral oedema

Rare: Hyponatraemia

Very rare: Hypomagnesaemia

Psychiatric disorders:

Uncommon: Insomnia

Rare: Agitation, confusion, depression

Very rare: Aggression, hallucination

Nervous system disorders:

Common: Headache

Uncommon: Dizziness, paraesthesia, somnolence

Rare: Taste disturbance

Eye disorders:

Rare: Blurred vision

Ear and labyrinth disorders:

Uncommon: Vertigo

Respiratory, thoracic and mediastinal disorders:

Rare: Bronchospasm

Gastrointestinal disorders:

Common: Abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation

Uncommon: Dry mouth

Rare: Stomatitis, gastrointestinal candidiasis, gastrointestinal infections

Very rare: Microscopic colitis

Hepatobiliary disorders:

Uncommon: Increased liver enzymes

Rare: Hepatitis with or without jaundice

Very rare: Hepatic encephalopathy

Skin and subcutaneous tissue disorders:

Uncommon: Dermatitis, pruritus, urticaria, rash

Rare: Alopecia, photosensitivity

Musculoskeletal, connective tissue and bone disorders:

Rare: Arthralgia, myalgia

Reproductive system and breast disorders:

Very rare: Gynaecomastia

General disorders and administration site conditions:

Rare: Malaise, hyperhidrosis

Post marketing experience:

The following adverse events have been reported during the post marketing use of NEXIAM. Because these are spontaneous reports from a population of uncertain size, it is not possible to reliably estimate their frequency.

Blood and lymphatic system disorders:

Leukopenia, thrombocytopenia, agranulocytosis, pancytopenia

Immune system disorders:

Hypersensitivity reactions e.g. angioedema and anaphylactic reaction/shock

Metabolism and nutrition disorders:

Peripheral oedema, hyponatraemia

Psychiatric disorders:

Insomnia, agitation, confusion, depression, aggression, hallucination

Nervous system disorders:

Headache, dizziness, paraesthesia, somnolence, taste disturbance

Eye disorders:

Blurred vision

Ear and labyrinth disorders:

Vertigo

Respiratory, thoracic and mediastinal disorders:

Bronchospasm

Gastrointestinal disorders:

Abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation, dry mouth, stomatitis, gastrointestinal candidiasis

Hepatobiliary disorders:

Increased liver enzymes, hepatitis with or without jaundice, hepatic encephalopathy, hepatic failure

Skin and subcutaneous tissue disorders:

Dermatitis, pruritus, urticaria, rash, alopecia, photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN)

Musculoskeletal, connective tissue and bone disorders:

Arthralgia, myalgia, muscular weakness

Renal and urinary disorders:

Interstitial nephritis

Reproductive system and breast disorders:

Gynaecomastia

General disorders and administration site conditions:

Malaise, hyperhidrosis

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

No specific antidote is known. NEXIAM is extensively plasma protein bound and is therefore not readily dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

IDENTIFICATION:

NEXIAM 20 mg:

A light pink, oblong, biconvex, film-coated tablet engraved 20 mg on one side and A/EH on the other side.

NEXIAM 40 mg:

A pink, oblong, biconvex, film-coated tablet engraved 40 mg on one side and A/EI on the other side.

NEXIAM 10 mg Sachets:

Pale yellow fine granules in a unit dose sachet. Brownish granules may be visible.

Reconstituted suspension: The oral suspension is a thick yellow liquid containing suspended pellets.

PRESENTATION:

NEXIAM 20 and 40 mg tablets:

White HDPE bottles (with desiccated caps) of 2, 5, 7, 14, 15, 28, 30, 56, 60, 100 tablets.

PVC/aluminium blister packages of 3, 7, 14, 15, 28, 30, 50, 56, 60, 98, 100 tablets.

NEXIAM 10 mg Sachets:

The esomeprazole pellets and excipient granules are packed into a sachet made out of 3 layers of an aluminium laminate.

Carton containing 28 sachets.

STORAGE INSTRUCTIONS:

NEXIAM 20 and 40 mg tablets:

Store at or below 30 °C. Store in a dry place. Keep the container tightly closed (bottle).

NEXIAM 10 mg Sachets:

Store at or below 25 °C. Do not open the sachets until prior to use.

Reconstituted suspension must be taken within 30 minutes after reconstitution.

Keep out of reach of children.

REGISTRATION NUMBERS:

NEXIAM 20 mg:	35/11.4.3/0263
NEXIAM 40 mg:	35/11.4.3/0264
NEXIAM 10 mg Sachets:	42/11.4.3/1003

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTATION:

AstraZeneca Pharmaceuticals (Pty) Limited

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Johannesburg,

2021

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CDS: Dec 2007, Jun 2009, Aug 2009, Jan 2010, May 2010, May 2011, Jan 2012

Nexiam 20 mg	Nexiam 40 mg	Nexiam 10 mg Sachets
NAMIBIA: NS2	NAMIBIA: NS2	NAMIBIA: NS2
Reg. No.: 04/11.4.3/1811	Reg. No.: 04/11.4.3/1810	Reg. No.: 12/11.4.3/0017

Nexiam 20 mg	Nexiam 40 mg
BOTSWANA: S2	BOTSWANA: S2
Reg. No.: BOT 0700958	Reg. No.: BOT 0600872