SUMMARY OF PRODUCT CHARACTERISTICS
NEBIGOOD AM (Nebivolol / Amlodipine Film-Coated Tablets)

1. NAME OF THE MEDICINAL PRODUCT

NEBIGOOD AM (Nebivolol 5 mg / Amlodipine 5 mg Film-Coated Tablets)

(Strength/composition to be confirmed by applicant from approved CTD dossier)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains nebivolol 5 mg (as nebivolol hydrochloride) and amlodipine 5 mg (as amlodipine besylate USP).

Excipients with known effect:

Contains lactose. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

(Tablet description to be confirmed by applicant from approved CTD dossier.)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NEBIGOOD AM is indicated for the treatment of essential hypertension in adults as a substitute therapy in patients already controlled on nebivolol and amlodipine given concurrently at the same doses.

4.2 Posology and method of administration

Adults

One tablet once daily. This fixed-dose combination is indicated only for patients whose blood pressure is already controlled on nebivolol and amlodipine administered as separate tablets at equivalent doses.

Elderly (>65 years)

The same dose should be used with caution. Nebivolol clearance is reduced in elderly patients; dose selection should be cautious, generally starting at the lower end of the dosing range.

Renal impairment

No dose adjustment required in mild to moderate renal impairment. For severe renal impairment, the starting dose for nebivolol should be 2.5 mg daily and the combination may not be appropriate — individual component titration is recommended.

Hepatic impairment

NEBIGOOD AM is contraindicated in patients with hepatic impairment or hepatic insufficiency (see section 4.3).

Paediatric population

The safety and efficacy in children and adolescents have not been established.

Method of administration

Oral. May be taken with or without food.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Liver disease or hepatic impairment.
- Severe bradycardia (heart rate <60 bpm).
- Sick sinus syndrome, sinoatrial block, second or third degree AV block without a pacemaker.
- Cardiogenic shock.
- Decompensated heart failure requiring IV inotropic therapy.

- Severe asthma or severe chronic obstructive pulmonary disease (COPD).
- Untreated phaeochromocytoma.
- Metabolic acidosis.
- Peripheral vascular disease with critical limb ischaemia.
- Severe hypotension (SBP <90 mmHg).

4.4 Special warnings and precautions for use

Cardiac effects

Beta-blockers may cause bradycardia and should be used with caution in patients with first-degree AV block. If heart rate falls below 55–60 bpm in resting conditions, and the patient experiences symptoms related to bradycardia, the dose should be reduced. Nebivolol must not be used in patients with acute or decompensated heart failure requiring IV inotropic therapy. In chronic stable heart failure, nebivolol should be introduced with caution, starting with a very low dose and under close medical supervision.

Nebivolol and other beta-blockers may unmask or exacerbate symptoms of peripheral arterial circulatory disorders (e.g. Raynaud's disease). Nebivolol must not be abruptly discontinued, especially in ischaemic heart disease patients; withdrawal should be gradual over 1–2 weeks.

Respiratory effects

Nebivolol should not be used in patients with bronchospastic disorders. Although highly cardioselective (β1-selective), nebivolol can cause bronchospasm, which should be treated with a bronchodilator.

Amlodipine — heart failure

Amlodipine should be used with caution in patients with heart failure. In long-term, placebo-controlled studies in patients with severe heart failure (NYHA III and IV), a higher rate of pulmonary oedema was observed with amlodipine.

Amlodipine — hepatic impairment

As amlodipine is extensively metabolised by the liver, the half-life will be prolonged in patients with impaired liver function. This combination is contraindicated in hepatic impairment.

Hyperkalaemia and potassium monitoring

Beta-blockers may raise serum potassium levels. Monitor potassium in patients at risk.

Diabetes mellitus

Nebivolol should be used with caution in diabetic patients as it may mask some symptoms of hypoglycaemia (tachycardia). The glycaemic control response and recognition of hypoglycaemia may be impaired; regular blood glucose monitoring is recommended.

Phaeochromocytoma

In patients with phaeochromocytoma, nebivolol should only be given after adequate alpha-blockade.

Psoriasis

Beta-blockers may provoke or exacerbate psoriasis.

Thyrotoxicosis

Beta-blockers may mask the signs of thyrotoxicosis.

Anaesthesia

In patients undergoing major surgery, beta-blockers should ideally not be discontinued; if they are, the anaesthetist should be informed. During anaesthesia, beta-blockers reduce the reflex tachycardia and increase the risk of hypotension.

Lactose content

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

4.5 Interaction with other medicinal products and other forms of interaction

Nebivolol interactions

Antiarrhythmics class I (quinidine, disopyramide) and class III (amiodarone, sotalol):

These combinations may potentiate the effect of nebivolol on heart rate and AV conduction.

Verapamil, diltiazem (calcium channel blockers with negative chronotropic effects):

Concomitant use may cause cardiac depression — particularly not recommended with IV verapamil.

Clonidine:

Abrupt withdrawal of clonidine in patients also taking beta-blockers may cause severe rebound hypertension; beta-blockers should be tapered before withdrawal of clonidine.

MAOIs:

Except MAO-B inhibitors — contraindicated; risk of hypertensive crisis.

Sympathomimetic agents:

May counteract the effect of nebivolol on blood pressure.

Antidiabetic agents (insulin, oral hypoglycaemics):

Nebivolol may enhance blood-glucose-lowering effects and mask signs of hypoglycaemia.

CYP2D6 inhibitors (fluoxetine, paroxetine, thioridazine, quinidine):

Nebivolol is predominantly metabolised by CYP2D6; strong inhibitors may increase nebivolol exposure.

Amlodipine interactions

CYP3A4 inhibitors (clarithromycin, itraconazole, ritonavir, grapefruit juice):

May increase amlodipine plasma concentrations and risk of adverse effects, including hypotension. Monitor blood pressure.

CYP3A4 inducers (rifampicin, St. John's Wort):

May decrease amlodipine plasma concentrations, reducing antihypertensive effect.

Ciclosporin and tacrolimus:

Amlodipine may increase plasma concentrations of ciclosporin and tacrolimus; monitor levels.

Simvastatin:

Co-administration of amlodipine 10 mg with simvastatin 80 mg increased simvastatin exposure by 77% — limit simvastatin to 20 mg/day with amlodipine.

Sildenafil:

Additive hypotensive effects; use with caution.

4.6 Fertility, pregnancy and lactation

Pregnancy

Nebivolol: beta-blockers reduce placental perfusion, which may result in intrauterine death, preterm birth, and neonatal bradycardia, hypoglycaemia and respiratory depression. Not recommended during pregnancy unless clearly necessary. If treatment is essential, uteroplacental blood flow and foetal growth should be monitored.

Amlodipine: limited data in pregnant women. In animal studies, reproductive toxicity was observed at high doses. Use in pregnancy only when the benefit clearly outweighs the risk.

This combination is not recommended during pregnancy; the benefit/risk ratio should be carefully evaluated before use.

Breast-feeding

It is not known whether nebivolol or amlodipine are excreted in human milk. Because of the potential risk for adverse reactions in the breast-fed infant, this combination should not be used during breast-feeding.

Fertility

There are no clinical data on the effect of this combination on human fertility.

4.7 Effects on ability to drive and use machines

NEBIGOOD AM may affect the ability to drive or operate machines. Dizziness and fatigue have been reported with nebivolol; dizziness, headache and somnolence with amlodipine. Patients should be cautioned accordingly, particularly during initiation of treatment or after a dose increase.

4.8 Undesirable effects

Nebivolol — selected adverse reactions

Very common: headache. Common: dizziness, paresthesia, dyspnoea, constipation, nausea, diarrhoea, fatigue, oedema. Uncommon: nightmares, depression, syncope, vision disturbance, bradycardia, acute heart failure, hypotension, peripheral oedema, impotence, rash, pruritus. Rare: AV block, bronchospasm. Not known: hypersensitivity reactions.

Amlodipine — selected adverse reactions

Very common: oedema. Common: somnolence, dizziness, headache, palpitations, flushing, abdominal pain, nausea, ankle swelling, fatigue. Uncommon: insomnia, mood changes, tremor, dysgeusia, syncope, visual disturbances, tinnitus, hypotension, dyspnoea, vomiting, pruritus, rash, alopecia, urticaria, back pain, muscle cramps, myalgia, micturition disorders, impotence, weight gain. Rare: peripheral neuropathy, depression, hepatitis, jaundice. Very rare: gynecomastia, hyperglycaemia, thrombocytopenic purpura.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority.

4.9 Overdose

Symptoms
Nebivolol overdose: bradycardia, hypotension, bronchospasm, acute cardiac insufficiency, hypoglycaemia. Amlodipine overdose: marked peripheral vasodilation with reflex tachycardia and possibly significant and potentially prolonged systemic hypotension.

Treatment
Symptomatic and supportive treatment. Gastric lavage if appropriate. For bradycardia: atropine; for heart failure: diuretics and vasopressors; glucagon may be used for beta-blocker overdose. For amlodipine overdose: IV calcium gluconate; vasopressors (dopamine/dobutamine) may be required. Cardiac monitoring should be maintained. Due to the high protein binding of amlodipine, dialysis is unlikely to be beneficial.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta-blocking agents, selective, combinations. ATC code: C07FB12.

Nebivolol is a highly selective β1-adrenoreceptor blocking agent with mild vasodilatory properties mediated through the L-arginine/nitric oxide (NO) pathway. Nebivolol reduces heart rate and myocardial contractility, decreasing cardiac output. The vasodilatory component (via NO release) counteracts the reflex increase in peripheral vascular resistance seen with non-vasodilatory beta-blockers.

Amlodipine is a dihydropyridine calcium channel antagonist (calcium ion antagonist / slow channel blocker) that inhibits the transmembrane influx of calcium ions into cardiac and smooth muscle cells. The antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle.

The combination of nebivolol and amlodipine provides complementary mechanisms of blood pressure reduction: nebivolol primarily reduces heart rate and cardiac output, while amlodipine reduces peripheral vascular resistance. The combination provides additive antihypertensive efficacy.

5.2 Pharmacokinetic properties

Nebivolol
Nebivolol is rapidly absorbed after oral administration. It undergoes first-pass metabolism. There are two phenotypes: fast metabolisers (majority of the population; elimination half-life ~10 hours) and slow metabolisers (~5% of the Caucasian population; half-life ~30 hours). Plasma protein binding approximately 98%. Nebivolol is metabolised by aromatic hydroxylation (CYP2D6) and glucurono-conjugation; the active d-nebivolol and its metabolites are excreted renally and in the faeces.

Amlodipine
Slowly and almost completely absorbed after oral administration; bioavailability approximately 64–80%. Peak plasma concentrations in 6–12 hours. Extensively bound to plasma proteins (approximately 97.5%). Eliminated primarily by hepatic metabolism to inactive metabolites; ~10% of parent compound and 60% of metabolites excreted in urine. Terminal elimination half-life approximately 35–50 hours. No dose adjustment required in renal impairment.

5.3 Preclinical safety data

Non-clinical data for both components individually reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. In reproductive toxicity studies, beta-blockers as a class reduce placental perfusion and may affect foetal development; amlodipine produced developmental toxicity in animal studies only at doses producing maternal toxicity. A safety evaluation of the combination at clinical ratios has not been separately reported.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose (excipient with known effect), microcrystalline cellulose, purified talc, magnesium stearate, colloidal anhydrous silica, croscarmellose sodium, and tablet coat components.

(Full excipient list to be confirmed by applicant from approved CTD dossier.)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C. Keep out of the reach and sight of children.

6.5 Nature and contents of container

ALU-ALU blister packs in unit box with leaflet insert. Pack size: 30 tablets (3×10).

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

ZAIN PHARMA LTD.

Plot No. 209/13741, Colchester Park,

Go-Down No. 1, 2, 3, Off Mombasa Road,

Behind Nice and Lovely House,

P.O. Box: 100167-00101, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

H2026/CTD11871/25344

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

06.01.2026

10. DATE OF REVISION OF THE TEXT

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