SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NEBIGOOD AM-H Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Tablet contains:

Nebivolol Hydrochloride

Eq.to Nebivolol 5mg

Amlodipine besylate USP

Eq.to Amlodipine 5mg

Hydrochlorothiazide USP 12.5 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White , round shape flat uncoated tablets having breakline on on side and other side plain

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nebivilol 5 mg, Amlodipine 5 mg & Hydrochlorothiazide 12.5 mg Tablets is a medicine used to treat hypertension (high blood pressure). This combination medicine controls blood pressure when a single medication is not effective. By lowering the blood pressure, it helps in preventing future heart attack and stroke.

4.2 Posology and method of administration

Posology

The dose is one tablet daily, preferably at the same time of the day. Tablets may be taken with meals.

Elderly

In view of the limited experience in patients above 75 years, caution must be exercised and these patients monitored closely.

Renal impairment

Nebevilol 5 mg, Amlodipine 5 mg & Hydrochlorothiazide 12.5 mg Tablet should not be given to patients with severe renal insufficiency

Hepatic impairment

Data in patients with hepatic insufficiency or impaired liver function are limited. Therefore the use of Nebevilol 5 mg, Amlodipine 5 mg & Hydrochlorothiazide 12.5 mg Tablet in these patients is contraindicated.

Paediatric population

The efficacy and safety of Nebevilol 5 mg, Amlodipine 5 mg & Hydrochlorothiazide 12.5 mg Tablet in children and adolescents aged below 18 years has not been established. No data are available. Therefore, use in children and adolescents is not recommended.

Method of administration

Oral use

Tablets may be taken with meals.

4.3 Contraindications

- Hypersensitivity to the active substances
- Hypersensitivity to other sulphonamide-derived substances (since hydrochlorothiazide is a sulphonamide-derived medicinal product)
- Liver insufficiency or liver function impairment
- Anuria, severe renal insufficiency (creatinine clearance < 30 ml/min)
- Acute heart failure, cardiogenic shock or episodes of heart failure decompensation requiring intravenous inotropic therapy
- Sick sinus syndrome, including sino-atrial block
- Second and third degree atrioventricular block (without a pacemaker).

• Bradycardia (heart rate < 60 bpm prior to start therapy)

• Hypotension (systolic blood pressure < 90 mmHg)

• Severe peripheral circulatory disturbances

• History of bronchospasm and bronchial asthma

• Untreated phaeochromocytoma

• Metabolic acidosis

• Refractory hypokalaemia, hypercalcaemia, hyponatraemia and symptomatic hyperuricaemia

4.4 Special warnings and precautions for use

Nebivolol

The following warnings and precautions apply to beta-adrenergic antagonists in general.

Anesthesia:

Continuation of beta-blockade reduces the risk of arrhythmias during induction and intubation. If beta-blockade is interrupted in preparation for surgery, the beta-adrenergic antagonist should be discontinued at least 24 hours beforehand.

Caution should be observed with certain anesthetics that cause myocardial depression. The patient can be protected against vagal reactions by intravenous administration of atropine.

Cardiovascular:

General, beta-adrenergic antagonists should not be used in patients with untreated congestive heart failure (CHF), unless their condition has been stabilised. In patients with ischaemic heart disease, treatment with a beta-adrenergic antagonist should be discontinued gradually, i.e. over 1-2 weeks. If necessary replacement therapy should be initiated at the same time, to prevent exacerbation of angina pectoris.

Metabolic/endocrinological:

Nebivolol does not affect glucose levels in diabetic patients. Care should be taken in diabetic patients however, as nebivolol may mask certain symptoms of hypoglycaemia (tachycardia, palpitations).

Respiratory:

In patients with chronic obstructive pulmonary disorders, beta-adrenergic antagonists should be used with caution as airway constriction may be aggravated.

Hydrochlorothiazide

Renal impairment

Full benefit from thiazide diuretics can be derived only if the kidney function is not altered. In patients with renal disease, thiazides may increase azotaemia. Cumulative effects of this active substance may develop in patients with impaired renal function. If progressive renal impairment becomes evident, as indicated by arising non-protein nitrogen, careful reappraisal of therapy is necessary, with consideration given to discontinuing diuretic therapy

Metabolic and endocrine effects

Thiazide therapy may impair glucose tolerance. Dosage adjustments of insulin or oral hypoglycaemic agents may be required. Latent diabetes mellitus may become manifest during thiazide therapy.

Electrolyte imbalance

As for any patient receiving diuretic therapy, periodic determination of serum electrolytes should be performed at appropriate intervals.

Amlodipine

Use in patients with heart failure.

Patients with heart failure should be treated with caution. In a long-term, placebo-controlled study in patients with severe heart failure (NYHA class III and IV) the reported incidence of pulmonary oedema was higher in the amlodipine treated group than in the placebo group. Calcium channel blockers, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality.

Use in patients with impaired hepatic function

As with all calcium antagonists, amlodipine's half-life is prolonged and AUC values are higher in patients with impaired liver function and dosage recommendations have not been established. The drug should therefore be administered with caution in these patients.

Amlodipine should therefore be initiated at the lower end of the dosing range and caution should be used, both on initial treatment and when increasing the dose. Slow dose titration and careful monitoring may be required in patients with severe hepatic impairment.

4.5 Interaction with other medicinal products and other forms of interaction

All drugs interact differently for person to person. You should check all the possible interactions with your doctor before starting any medicine.

Interaction with Medicine

Diltiazem: Severe Fluoxetine: Moderate Itraconazole: Severe Amiodarone: Moderate Rifampicin: Severe Aminophylline: Severe Disease

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of Nebevilol 5 mg, Amlodipine 5 mg & Hydrochlorothiazide 12.5 mg Tablet in pregnant women. Animal studies on the two individual components are insufficient with respect to the effects of the combination of Nebevilol and hydrochlorothiazide on reproduction.

Breast-feeding

It is unknown whether Nebevilol is excreted into human breast milk. Animal studies have shown that Nebevilol is excreted into breast milk. Most beta-blockers, particularly lipophilic compounds like Nebevilol and its active metabolites, pass into breast milk although to a variable extent. Hydrochlorothiazide is excreted in human milk in small amounts. Thiazides in high doses causing intense diuresis can inhibit the milk production. The use of Nebevilol 5 mg, Amlodipine 5 mg & Hydrochlorothiazide 12.5 mg Tablet during breast-feeding is not recommended.

4.8 Undesirable effects

Common: headache, dizziness, paraesthesia Visual disturbance Palpitations, Dyspnea, Respiratory distress, pneumonitis, interstitial lung disease, pulmonary oedema, constipation, nausea, diarrhoea

Uncommon: Nightmares; depression, Depression, mood changes (including anxiety), insomnia, Tremor, dysgeusia, syncope, hypoaesthesia, paraesthesia impaired vision, bradycardia, heart failure, slowed AV conduction/AVblock, hypotension, (increase of) intermittent claudication, bronchospasm, dyspepsia, flatulence, vomiting, pruritus, rash erythematous, impotence

Rare: Allergic reactions

Very rare: Angioneurotic oedema, hypersensitivity, metabolic alkalosis, Syncope, Hypertonia, peripheral neuropathy, psoriasis aggravated

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorisation holder or, where applicable, via the national reporting system.

4.9 Overdose

Nebevilol:

Symptoms

No data are available on overdosage with Nebevilol. Symptoms of overdosage with beta-blockers are: bradycardia, hypotension, bronchospasm and acute cardiac insufficiency.

Treatment

In case of overdosage or hypersensitivity, the patient should be kept under close supervision and be treated in an intensive care ward. Blood glucose levels should be checked. Serum electrolytes and creatinine should be monitored frequently.

Hydrochlorothiazide:

Symptoms

Over dosage with hydrochlorothiazide is associated with electrolyte depletion (hypokalaemia, hypochloraemia, hyponatraemia) and dehydration resulting from excessive diuresis. The most common signs and symptoms of overdosage with hydrochlorothiazide are nausea and somnolence. Hypokalaemia may result in muscle spasm and/or accentuate cardiac arrhythmias associated with the concomitant use of digitalis glycosides or certain anti-arrhythmic medicinal products.

Treatment

In case of overdosage or hypersensitivity, the patient should be kept under close supervision and be treated in an intensive care ward. Blood glucose levels should be checked. Serum electrolytes and creatinine should be monitored frequently. Absorption of any drug residues still present in the gastro-intestinal tract can be prevented by gastric lavage and the administration of activated charcoal and a laxative. Artificial respiration may be required. Bradycardia or extensive vagal reactions should be treated by administering atropine or methylatropine. Hypotension and shock should be treated with plasma/plasma substitutes and, if necessary, catecholamines.

Amlodipine:

Symptoms

Available data suggest that gross over dosage could result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and probably prolonged systemic hypotension up to and including shock with fatal outcome have been reported.

Treatment

Administration of activated charcoal to healthy volunteers immediately or up to two hours after ingestion of amlodipine 10mg has been shown to significantly decrease amlodipine absorption.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Nebevilol:

Pharmacotherapeutic group: Beta blocking agent, selective. ATC code: C07AB12

Nebivolol is a racemate of two enantiomers, SRRR-nebivolol (or d-nebivolol) and RSSS-nebivolol (or l- nebivolol). It is a competitive and selective beta-receptor antagonist, due to the SRRRenatiomer (d- enantiomer), and also it has mild vasodilating properties due to an interaction with the L- arginine/nitric oxide pathway.

Amlodipine:

Pharmacotherapeutic group: Calcium channel blockers, selective calcium channel blockers with mainly vascular effects;

ATC code: C 08 CA 01

Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle.

Hydrochlorothiazide,

Pharmacotherapeutic group: Low-ceiling diuretics, thiazides – Thiazides, plain –Thiazide diuretics particularly exert their effect in the distal part of the renal tubule by inhibiting NaCl resorption (by antagonism of the Na+Cl carrier).

ATC code: C03AA03.

The increased amount of Na+ and water in the ductus colligens (collecting duct) and/or the increased filtration rate results in an increase in the secretion and excretion of K+ and H+ . In people with normal renal function, diuresis is already promoted after administration of 12.5 mg of hydrochlorothiazide. The resulting increase in the urinary excretion of sodium and chloride and the relatively small increase in potassium in the urine are dose related. The diuretic and natriuretic effect is noticeable after 1–2 hours following the oral administration of hydrochlorothiazide, reaches its maximum after 4–6 hours and can last for 10–12 hours. Thiazide-induced diuresis initially results in a decrease in plasma volume, the cardiac minute volume and systemic blood pressure. The renin-angiotensin-aldosterone system can be activated. The hypotensive effect continues to be maintained with the continuation of the medication, probably as a result of the decrease in peripheral resistance; the cardiac minute volume returns to the original value and the plasma volume remains somewhat lower. With long-term administration, the antihypertensive effect of hydrochlorothiazide is dose related between 12.5 and 50 mg a day. The maximum hypotensive effect is usually reached at 50 mg a day in most patients. Increasing the dose to above 50 mg/day increases the metabolic complications and is rarely necessary from a therapeutic point of view. If given as a monotherapy, hydrochlorothiazide appears to produce a good effect in around 40–50% of patients, just like other diuretics. In general, elderly people and black people appear to respond well to diuretics as the primary therapy. Combined treatment with other antihypertensive agents increases the blood pressure lowering effect. In a large proportion of patients who show an unsatisfactory response to a monotherapy, a further decrease in blood pressure can be achieved in this way. As thiazide diuretics such as hydrochlorothiazide reduce Ca+ excretion, these are used in order to prevent the recurrence of renal calcium oxalate stones in patients with idiopathic normocalcaemic hypercalciuria. With long-term treatment, users of thiazide diuretics appear to have a significantly higher mineral content in their bones than non-users. In nephrogenic diabetes insipidus, hydrochlorothiazide reduces the volume of urine and increases the osmolality of the urine.

5.2 Pharmacokinetic properties

Nebivolol:

Both nebivolol enantiomers are rapidly absorbed after oral administration. The absorption of nebivolol is not affected by food. It can be given with or without meals.

Nebivolol is extensively metabolised, partly to active hydroxy-metabolites. Nebivolol is metabolised via alicyclic and aromatic hydroxylation, N-dealkylation and glucuronidation. In addition, glucuronides of the hydroxy-metabolites are formed. The metabolism of nebivolol by aromatic hydroxylation is subject to the CYP2D6 dependent genetic oxidative polymorphism. The oral bioavailability of nebivolol averages 12% in fast metabolizing patients and is virtually complete in slow metabolisers.

Amlodipine:

Absorption, distribution, plasma protein binding:

After oral administration of therapeutic doses, amlodipine is well absorbed with peak blood levels between 6-12 hours post dose. Absolute bioavailability has been estimated to be between 64 and 80%. The volume of distribution is approximately 21 l/kg. In vitro studies have shown that approximately 97.5% of circulating amlodipine is bound to plasma proteins.

Hydrochlorothiazide :

Absorption :The absorption of hydrochlorothiazide administered as hydrochlorothiazide tablets amounts in total to around 70% of the dose. However, variations in absorption as a result of fasting or the intake of food are of little clinical significance. The absorption of hydrochlorothiazide is reduced in patients who suffer from cardiac decompensation. In the therapeutic domain, the bioavailability and maximum concentration are directly proportional to the dose. After continuous administration, the pharmacokinetics of hydrochlorothiazide do not change and the average concentration is around 100 ng/ml at a dose of 75 mg a day every day for six weeks.

Distribution : Hydrochlorothiazide accumulates in erythrocytes and reaches a maximum concentration around 4 hours after oral administration. After 10 hours, the concentration in the erythrocytes is around three times higher than in the plasma. Binding to plasma proteins of around 40–70% has been reported and the apparent volume of distribution can be estimated to be 5–6 l/kg. Hydrochlorothiazide crosses the placenta and, in the umbilical cord, reaches a concentration which approaches the concentration in the plasma of the mother. The medicinal product accumulates in the amniotic fluid, where the concentration can be nineteen times the concentration in the umbilical cord. Hydrochlorothiazide is excreted in the maternal milk.

Elimination : Hydrochlorothiazide is eliminated from plasma with an elimination half-life of on average 9.5 to 13 hours in the terminal elimination phase. Within 72 hours, 60–80% of an oral dose is excreted in the urine, 95% in an unchanged form and around 4% in the form of the hydrolysate 2-amino-4-chloro-mbenzene disulphonamide (ACBS). Up to 24% of an oral dose is excreted in the faeces and a negligible amount is excreted via bile. In elderly patients, the “steady-state” concentration of hydrochlorothiazide is elevated and systemic clearance is significantly decreased compared with younger patients. For this reason, it is necessary that the treatment of elderly patients take place under strict supervision. In patients with renal impairment (creatinine clearance between 30 and around 70 ml/min), the rate of urinary excretion is reduced and a higher maximum plasma concentration and AUC are observed. The average elimination half-life is twice as long. Hepatic diseases do not have a significant influence on the pharmacokinetics of hydrochlorothiazide however caution is recommended when hydrochlorothiazide is administered to patients with liver disease.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of genotoxicity , reproductive and developmental toxicity and carcinogenic potential.

Adverse effects on the reproductive function were only recorded at high doses, exceeding by several fold the maximum recommended human dose (see Section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List Of Excipients

*Maize Starch

Lactose

Microcrystalline Cellulose

Povidone K 30

**Purified water

Purified talc

Magnesium Stearate

Colloidal Ahydrous Silica

Cross carmelose sodium

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

10 tablets are packed in ALU-ALU blister, such 3 blisters are packed in one carton with insert coded with batch number, manufacturing date and expiry date.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

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

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER 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
H2026/CTD12001/25342

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION
18/02/2026

10. DATE OF REVISION OF THE TEXT

18/02/2026