SUMMARY OF PRODUCT CHARACTERISTICS
TRIOGOOD 20 (Aspirin 75 mg, Clopidogrel 75 mg & Atorvastatin 20 mg Capsules)

1. NAME OF THE MEDICINAL PRODUCT

TRIOGOOD 20 (Aspirin 75 mg / Clopidogrel 75 mg / Atorvastatin 20 mg Hard Gelatine Capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatine capsule contains:

Atorvastatin calcium USP equivalent to atorvastatin 20 mg (as pellets)

Clopidogrel bisulphate USP equivalent to clopidogrel 75 mg (as pellets)

Aspirin USP 75 mg (as enteric-coated pellets)

Excipients with known effect:

None

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard gelatine capsule.

Light green opaque cap / clear body, size '0' hard gelatine capsule containing white, red and green pellets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TRIOGOOD 20 is indicated for secondary prevention of atherothrombotic events in adult patients who are already taking aspirin, clopidogrel and atorvastatin as separate tablets, where switching to this fixed-dose combination is clinically appropriate. It reduces the risk of cardiovascular death, myocardial infarction and stroke in patients with acute coronary syndrome or established coronary artery disease, in combination with lipid-lowering therapy with atorvastatin.

4.2 Posology and method of administration

Adults

One capsule once daily. The capsule should be taken with water and may be taken with or after meals. Due to the enteric-coated aspirin pellets, capsules should be swallowed whole and not opened or crushed.

Missed dose

If a dose is missed, the patient should take the next dose at the scheduled time and should not double the dose.

Elderly

No dose adjustment is required. The lowest effective dose should be used with appropriate monitoring.

Renal impairment

No specific dose adjustment is required for mild to moderate renal impairment. Aspirin and atorvastatin should be used with caution in severe renal impairment. Clopidogrel has not been studied in patients with severe renal impairment.

Hepatic impairment

This combination is contraindicated in active liver disease or unexplained persistent elevations of serum transaminases. Aspirin and clopidogrel should be used with caution in patients with hepatic impairment.

Paediatric population

The safety and efficacy in children and adolescents have not been established. This combination is not recommended in patients under 18 years of age.

4.3 Contraindications

- Hypersensitivity to aspirin, clopidogrel, atorvastatin or to any of the excipients listed in section 6.1.
- Active pathological bleeding (e.g. peptic ulcer or intracranial haemorrhage).

- History of asthma, urticaria or allergic-type reactions to acetylsalicylic acid or other NSAIDs (risk of cross-reactivity).
- Active liver disease or unexplained persistent elevations of serum transaminases exceeding 3× ULN.
- Pregnancy and breast-feeding (atorvastatin is contraindicated in pregnancy; aspirin at antiplatelet doses is not recommended in the third trimester).
- Concomitant administration of strong CYP3A4 inhibitors (e.g. ciclosporin, clarithromycin, certain HIV protease inhibitors such as nelfinavir) with atorvastatin, due to risk of myopathy/rhabdomyolysis.
- Concomitant use of omeprazole or esomeprazole with clopidogrel is not recommended, as these reduce the antiplatelet effect via CYP2C19 inhibition.

4.4 Special warnings and precautions for use

Bleeding risk

As with all antiplatelet/anticoagulant combinations, this product increases the risk of bleeding. Patients should be monitored for signs and symptoms of bleeding. The combination of aspirin and clopidogrel significantly reduces platelet aggregation and increases the risk of haemorrhage. Particular caution is needed in patients at risk of increased bleeding (trauma, surgery, etc.).

Atorvastatin — skeletal muscle effects

Myopathy (myalgia, myositis, rhabdomyolysis) has been reported with statins, particularly at higher doses or when combined with certain medicinal products. Patients should report unexplained muscle pain, tenderness or weakness promptly. CK levels should be measured if myopathy is suspected; treatment should be discontinued if CK is markedly elevated (>10× ULN) or if muscular symptoms are severe. Risk is increased in elderly patients (>70 years), patients with renal impairment, hypothyroidism, personal or family history of hereditary muscular disorder, prior history of muscle toxicity with statins or fibrates, and excessive alcohol intake. Atorvastatin must not be co-administered with systemic fusidic acid; if essential, statin treatment should be discontinued for the duration of fusidic acid treatment.

Atorvastatin — liver effects

Liver function tests should be performed before initiation and as clinically indicated. If transaminases rise to >3× ULN, the dose should be reduced or treatment discontinued. Atorvastatin should be used with caution in patients who consume substantial quantities of alcohol and/or with a history of liver disease.

Atorvastatin — diabetes mellitus

Some evidence suggests statins as a class raise blood glucose. Patients at risk of diabetes should be monitored; this risk is outweighed by the cardiovascular benefit of statin therapy.

Atorvastatin — severe cutaneous adverse reactions

Severe cutaneous adverse reactions including SJS and DRESS have been reported with atorvastatin. If signs or symptoms suggestive of SJS or DRESS appear, atorvastatin must be discontinued immediately and not restarted.

Clopidogrel — CYP2C19 poor metabolisers

Clopidogrel is a prodrug that requires CYP2C19-mediated conversion to its active metabolite. Poor metabolisers have reduced antiplatelet response. Testing for CYP2C19 genotype may be considered in patients at risk. Omeprazole, esomeprazole, and other strong CYP2C19 inhibitors should not be combined with clopidogrel as they reduce its antiplatelet effect.

Aspirin — GI effects

Aspirin may cause gastric mucosal damage and GI bleeding. Aspirin should be used with caution in patients with a history of peptic ulcer disease, GI bleeding, asthma, or glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Reye's syndrome

Aspirin should not be used in children and adolescents under 16 years with a viral illness due to risk of Reye's syndrome.

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin interactions

Other NSAIDs (including ibuprofen at anti-inflammatory doses): increased risk of GI bleeding and ulceration. Anticoagulants and other antiplatelet agents: increased risk of haemorrhage — close monitoring required. Corticosteroids: increased risk of GI ulceration. Methotrexate: NSAIDs may increase toxicity of methotrexate. SSRIs: increased risk of GI bleeding.

Clopidogrel interactions

Omeprazole/esomeprazole (not recommended): reduce active metabolite of clopidogrel by ~40–50% via CYP2C19 inhibition, reducing antiplatelet effect. Warfarin: concomitant use is not recommended as it may intensify bleeding. Other CYP2C8 substrates or inhibitors (e.g. repaglinide, gemfibrozil): exercise caution. Anticoagulants and NSAIDs: increased bleeding risk.

Atorvastatin interactions

Strong CYP3A4 inhibitors (clarithromycin, certain HIV protease inhibitors, itraconazole): increase atorvastatin plasma concentrations and risk of myopathy. These combinations are contraindicated with certain protease inhibitors; otherwise use with caution and limit atorvastatin dose. Ciclosporin (contraindicated with atorvastatin): greatly increases atorvastatin exposure. Gemfibrozil and other fibrates: increased risk of myopathy. Fusidic acid (systemic): must not be co-administered with atorvastatin. Digoxin: concomitant use may increase digoxin plasma concentrations; monitor. Oral contraceptives: concomitant use results in increased AUC of norethindrone and ethinyl estradiol.

4.6 Fertility, pregnancy and lactation

Pregnancy

Atorvastatin is contraindicated during pregnancy as inhibition of cholesterol biosynthesis may cause foetal harm. Women of childbearing potential must use appropriate contraceptive measures during treatment. Aspirin at antiplatelet doses should be avoided during the third trimester (risk of premature closure of the ductus arteriosus, maternal and neonatal bleeding). If pregnancy is detected, this combination should be discontinued immediately.

Breast-feeding

This combination should not be used during breast-feeding. Atorvastatin is excreted in rat milk; aspirin distributes into breast milk; safety data for clopidogrel in breast-feeding are insufficient.

Fertility

No data on the effect of this combination on human fertility. Atorvastatin did not affect fertility in animal studies at doses producing plasma AUC values up to 9 times the maximum recommended human dose.

4.7 Effects on ability to drive and use machines

Dizziness has been reported with clopidogrel and atorvastatin. Patients who experience dizziness should avoid driving or operating machinery.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse effects of this combination reflect the known profiles of its individual components. Aspirin: GI adverse effects (nausea, dyspepsia, epigastric pain), increased bleeding tendency, and rarely bronchospasm in aspirin-sensitive patients. Clopidogrel: bleeding (epistaxis, GI haemorrhage), GI effects (diarrhoea, abdominal pain), rash. Atorvastatin: myalgia, muscle weakness, elevated liver transaminases, nausea, diarrhoea, constipation, abdominal pain, headache.

System Organ Class	Common	Uncommon / Rare
Nervous system disorders	Headache, dizziness	Paraesthesia (uncommon)
Gastrointestinal disorders	Nausea, dyspepsia, diarrhoea, abdominal pain, constipation	GI bleeding, peptic ulcer, nausea, vomiting (uncommon/rare)
Blood and lymphatic disorders	Increased bleeding tendency	Thrombocytopenia, neutropenia (uncommon)
Respiratory disorders		Bronchospasm (in aspirin-sensitive patients, rare)
Musculoskeletal disorders	Myalgia	Myopathy, rhabdomyolysis (rare)
Hepatobiliary disorders	Elevated transaminases (uncommon)	Hepatitis, jaundice (rare)
Skin disorders	Rash, bruising	Urticaria, pruritus, DRESS, SJS (rare)
Immune disorders		Anaphylaxis (rare)

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

Aspirin: Salicylism — tinnitus, dizziness, hearing impairment, nausea, vomiting, respiratory alkalosis followed by metabolic acidosis. Clopidogrel: Bleeding complications. Atorvastatin: No specific overdose information available; supportive management recommended.

Treatment

Symptomatic and supportive treatment. For aspirin overdose, gastric lavage and alkalinisation of urine may enhance salicylate excretion. Monitor clotting parameters if bleeding occurs. There is no specific antidote for clopidogrel overdose; platelet transfusion may be considered. For atorvastatin, monitor liver function and CK levels. Haemodialysis is unlikely to be of benefit for any component.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Platelet aggregation inhibitors excluding heparin, combinations. ATC code: C10BX.

Aspirin (acetylsalicylic acid):

Irreversibly inhibits cyclooxygenase (COX-1) in platelets, preventing thromboxane A2 synthesis and thereby inhibiting platelet aggregation. At low doses (75 mg), it is used as an antiplatelet agent.

Clopidogrel:

A thienopyridine prodrug that requires hepatic CYP2C19-mediated bioactivation to an active thiol metabolite. The active metabolite irreversibly binds to the P2Y12 ADP receptor on platelets, preventing ADP-mediated activation of the GPIIb/IIIa complex and subsequent platelet aggregation. The antiplatelet effect is maintained for the platelet lifespan (~7–10 days).

Atorvastatin 20 mg:

A selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts HMG-CoA to mevalonate (a precursor of cholesterol). The primary site of action is the liver. Atorvastatin reduces LDL-cholesterol, total cholesterol, triglycerides, VLDL-cholesterol and increases HDL-cholesterol.

5.2 Pharmacokinetic properties

Aspirin

Rapidly absorbed from the stomach and intestine by passive diffusion. Transformed into the active metabolite salicylate in the stomach, intestinal mucosa, blood and liver. Salicylate binds extensively to albumin. Elimination is via renal excretion; at low antiplatelet doses, a large fraction of salicylate is conjugated with glycine (saturable pathway). The half-life of salicylate depends on dose due to non-linear kinetics. The aspirin component in this product is enteric-coated to minimise gastric mucosal exposure.

Clopidogrel

Approximately 50% absorbed following an oral dose of 75 mg. Clopidogrel is extensively metabolised in the liver by CYP2C19 and other CYP enzymes (CYP1A2, CYP2B6, CYP3A4). The active thiol metabolite reaches peak plasma concentration approximately 0.5–1 hour after dosing. At steady state (Day 9), the active metabolite achieves sustained platelet inhibition.

Atorvastatin

Atorvastatin presents a dose-dependent, non-linear pharmacokinetic profile. Rapidly absorbed after oral administration (Tmax 1–2 hours after a 40 mg dose). Absolute bioavailability is approximately 14% due to first-pass extraction. Extensively bound to plasma proteins (≥98%). Extensively metabolised to ortho- and parahydroxylated metabolites, all of which are pharmacologically active. Eliminated primarily via biliary excretion; the terminal half-life is approximately 14 hours (but HMG-CoA reductase inhibitory activity half-life ~20–30 hours). Systemic exposure of atorvastatin 20 mg is proportional to dose within the therapeutic range.

5.3 Preclinical safety data

Aspirin: Well-established safety profile; GI irritation, bleeding and allergic reactions are known risks. No evidence of carcinogenicity at therapeutic doses. Clopidogrel: Non-clinical studies demonstrated no genotoxic potential; no carcinogenic effects in rodents. Atorvastatin: No evidence of mutagenicity or clastogenicity. No

carcinogenic potential in rats or mice at systemic exposures approximately 16-fold and 6-fold the human AUC (10 mg/day), respectively. Skeletal muscle effects including rhabdomyolysis are known class effects of statins.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

(Excipient list to be completed by the applicant; the capsule fill contains aspirin enteric-coated pellets, clopidogrel pellets, and atorvastatin pellets in separate pellet populations within the hard gelatine shell. Individual pellet excipients should be declared.)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

10 capsules packed in one ALU-ALU blister; 3 such blisters packed in one printed and laminated carton with package insert. Pack size: 30 capsules.

6.6 Special precautions for disposal and other handling

Not applicable. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

PRO-MED PHARMACEUTICALS LTD

Old Mombasa Road, Behind Nice & Lovely Go-Downs,

Colchester Park Go-Downs,

P.O. Box 22953-00100, Nairobi, Kenya.

Manufacturer: ZAIN PHARMA LIMITED

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/CTD11883/25348

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

03.03.2026

10. DATE OF REVISION OF THE TEXT

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