Summary of Product Characteristics
CARDICLEAR 2.5
(Apixaban Film-coated Tablets 2.5 mg)

1. Name of the medicinal product

CARDICLEAR 2.5

Apixaban Film-coated Tablets 2.5 mg

2. Qualitative and quantitative composition

Each film-coated tablet contains 2.5 mg of apixaban.

Excipient with known effect
Each film-coated tablet contains lactose (as lactose monohydrate).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Yellow, round, biconvex film-coated tablets, plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age ≥ 75 years; hypertension; diabetes mellitus; or symptomatic heart failure (NYHA Class ≥ II).
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see section 4.4 for haemodynamically unstable PE patients).

4.2 Posology and method of administration

Posology

Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF)
The recommended dose of apixaban is 5 mg taken orally twice daily. A reduced dose of 2.5 mg twice daily is recommended in patients with NVAF and at least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL (133 micromole/L). Therapy should be continued long term.

Treatment of DVT, treatment of PE, and prevention of recurrent DVT and PE (VTEt)
The recommended dose for the treatment of acute DVT and treatment of PE is 10 mg taken orally twice daily for the first 7 days, followed by 5 mg taken orally twice daily. A short duration of treatment (at least 3 months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation). The

recommended dose for the prevention of recurrent DVT and PE is 2.5 mg taken orally twice daily, initiated following completion of 6 months of treatment with apixaban 5 mg twice daily or with another anticoagulant (see section 5.1).

Table 1. Dose recommendation (VTEt)

Indication	Dosing schedule	Maximum daily dose
Treatment of DVT or PE	10 mg twice daily for the first 7 days, followed by 5 mg twice daily	20 mg (first 7 days) then 10 mg
Prevention of recurrent DVT and/or PE following completion of 6 months of treatment for DVT or PE	2.5 mg twice daily	5 mg

The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk of bleeding (see section 4.4).

Missed dose

If a dose is missed, the patient should take apixaban immediately and then continue with twice-daily intake as before.

Switching

Switching from parenteral anticoagulants to apixaban (and vice versa) can be done at the next scheduled dose; these medicinal products should not be administered simultaneously. When converting from vitamin K antagonist (VKA) therapy, the VKA should be discontinued and apixaban started when the international normalised ratio (INR) is < 2.

Special populations

Renal impairment

In mild or moderate renal impairment: for VTEt, no dose adjustment is necessary; for NVAF, a dose reduction to 2.5 mg twice daily is required only where serum creatinine ≥ 1.5 mg/dL (133 micromole/L) is associated with age ≥ 80 years or body weight ≤ 60 kg. In severe renal impairment (creatinine clearance 15–29 mL/min): for VTEt, apixaban should be used with caution; for NVAF, patients should receive the lower dose of 2.5 mg twice daily. In patients with creatinine clearance < 15 mL/min or undergoing dialysis, apixaban is not recommended (see sections 4.4 and 5.2).

Hepatic impairment

Apixaban is contraindicated in patients with hepatic disease associated with coagulopathy and a clinically relevant bleeding risk (see section 4.3). It is not recommended in severe hepatic impairment, and should be used with caution in mild or moderate hepatic impairment (Child-Pugh A or B), where no dose adjustment is required. Patients with ALT/AST > 2 × ULN or total bilirubin ≥ 1.5 × ULN were excluded from clinical studies; liver function testing should be performed before initiation.

Elderly and body weight

No dose adjustment is required on the basis of age or body weight alone, unless the NVAF dose-reduction criteria are met.

Patients undergoing catheter ablation or cardioversion (NVAF)
Patients can continue apixaban while undergoing catheter ablation, and can remain on apixaban while being cardioverted; adherence should be confirmed before cardioversion.

Paediatric population
The safety and efficacy of apixaban in children and adolescents below 18 years of age have not been established.

Method of administration
For oral use. Apixaban should be swallowed with water, with or without food. For patients unable to swallow whole tablets, the tablets may be crushed and suspended in water, 5% glucose in water (G5W), apple juice, or mixed with apple puree, and administered immediately; alternatively, crushed tablets may be suspended in 60 mL of water or G5W and delivered immediately through a nasogastric tube. Crushed apixaban tablets are stable in water, G5W, apple juice and apple puree for up to 4 hours.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Active clinically significant bleeding.
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.
- A lesion or condition considered a significant risk factor for major bleeding — for example current or recent gastrointestinal ulceration, malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms, or major intraspinal or intracerebral vascular abnormalities.
- Concomitant treatment with any other anticoagulant (e.g. unfractionated heparin [UFH], low-molecular-weight heparins, heparin derivatives, or oral anticoagulants such as warfarin, rivaroxaban or dabigatran), except under the specific circumstances of switching anticoagulant therapy, when UFH is given at doses necessary to maintain a patent central venous or arterial catheter, or when UFH is given during catheter ablation for atrial fibrillation (see sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

Haemorrhage risk
As with other anticoagulants, patients taking apixaban should be observed carefully for signs of bleeding, and it should be used with caution in conditions with an increased risk of haemorrhage. Apixaban should be discontinued if

severe haemorrhage occurs. Although routine monitoring of exposure is not required, a calibrated quantitative anti-Factor Xa assay may be useful in exceptional situations (e.g. overdose or emergency surgery).

Interaction with medicinal products affecting haemostasis

Concomitant treatment with any other anticoagulant is contraindicated (see section 4.3). Concomitant use of antiplatelet agents increases the risk of bleeding, and care is required with concomitant SSRIs, SNRIs or NSAIDs (including acetylsalicylic acid, ASA). In a clinical study in atrial fibrillation, concomitant ASA increased the major bleeding risk on apixaban from 1.8% to 3.4% per year. A careful assessment of benefit against risk should be made before combining apixaban with mono or dual antiplatelet therapy.

Spinal / epidural anaesthesia or puncture

When neuraxial anaesthesia (spinal/epidural) or spinal/epidural puncture is employed, patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal haematoma, which can result in long-term or permanent paralysis. The risk may be increased by the use of indwelling epidural catheters or the concomitant use of other medicinal products affecting haemostasis. Patients should be monitored frequently for signs and symptoms of neurological impairment; if these occur, urgent diagnosis and treatment are necessary. An epidural catheter should not be removed earlier than 5 half-lives (approximately 24 to 30 hours) after the last apixaban dose, and the next dose should not be given earlier than 5 hours after catheter removal.

Prosthetic heart valves and antiphospholipid syndrome

Apixaban is not recommended in patients with prosthetic heart valves (with or without atrial fibrillation), as safety and efficacy have not been established. Direct-acting oral anticoagulants, including apixaban, are not recommended in patients with a history of thrombosis diagnosed with antiphospholipid syndrome, particularly triple-positive patients, in whom they may be associated with increased rates of recurrent thrombotic events compared with VKA therapy.

Surgery and invasive procedures

Apixaban should be discontinued at least 48 hours before elective surgery or invasive procedures with a moderate or high risk of bleeding, and at least 24 hours before those with a low bleeding risk. If the procedure cannot be delayed, appropriate caution should be exercised. In NVAF patients, bridging anticoagulation during the 24 to 48 hours after stopping apixaban is not generally required. Apixaban should be restarted as soon as the clinical situation allows and adequate haemostasis has been established. For catheter ablation, treatment does not need to be interrupted.

Haemodynamically unstable PE and active cancer

Apixaban is not recommended as an alternative to unfractionated heparin in patients with pulmonary embolism who are haemodynamically unstable or who

may receive thrombolysis or pulmonary embolectomy. Efficacy and safety of apixaban in the treatment of VTE in patients with active cancer have not been established.

Renal and hepatic impairment; elderly; low body weight

Apixaban plasma concentrations are increased in severe renal impairment (creatinine clearance 15–29 mL/min) and it should be used with caution or at the reduced dose as described in section 4.2; it is not recommended below 15 mL/min or in dialysis. Increasing age and low body weight (< 60 kg) may increase haemorrhagic risk. Apixaban is contraindicated in hepatic disease with coagulopathy, is not recommended in severe hepatic impairment, and should be used with caution in mild to moderate impairment.

Excipients

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

4.5 Interaction with other medicinal products and other forms of interaction

Inhibitors of CYP3A4 and P-gp

Co-administration with ketoconazole (a strong inhibitor of both CYP3A4 and P-gp) led to a 2-fold increase in mean apixaban AUC and a 1.6-fold increase in Cmax. Apixaban is not recommended in patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp, such as azole-antimycotics (ketoconazole, itraconazole, voriconazole, posaconazole) and HIV protease inhibitors (e.g. ritonavir). Agents that are not strong dual inhibitors (e.g. amiodarone, clarithromycin, diltiazem, fluconazole, naproxen, quinidine, verapamil) increase apixaban exposure to a lesser extent and require no dose adjustment; for example, diltiazem increased AUC 1.4-fold and naproxen 1.5-fold.

Inducers of CYP3A4 and P-gp

Co-administration with rifampicin (a strong inducer of both CYP3A4 and P-gp) decreased mean apixaban AUC and Cmax by approximately 54% and 42%. Other strong dual inducers (e.g. phenytoin, carbamazepine, phenobarbital, St John's wort) may similarly reduce apixaban concentrations. No dose adjustment is required, but apixaban should be used with caution for stroke/systemic embolism prevention in NVAF and for prevention of recurrent DVT/PE, and is not recommended for the treatment of DVT and PE, in patients receiving strong dual inducers, since efficacy may be compromised.

Anticoagulants, antiplatelets, SSRIs/SNRIs and NSAIDs

Concomitant treatment with any other anticoagulant is contraindicated (see section 4.3), except in the specific circumstances described. An additive effect on anti-Factor Xa activity was observed with enoxaparin. No relevant pharmacokinetic or pharmacodynamic interaction was evident with ASA,

clopidogrel, the clopidogrel/ASA combination, or prasugrel in Phase I studies. No clinically significant interactions were observed with atenolol or famotidine.

Effect of apixaban on other medicinal products

In vitro, apixaban showed no inhibition of CYP1A2, 2A6, 2B6, 2C8, 2C9, 2D6 or 3A4 and only weak inhibition of CYP2C19 at concentrations well above therapeutic peaks, and did not induce CYP1A2, 2B6 or 3A4/5. Apixaban did not affect the pharmacokinetics of digoxin, naproxen or atenolol, and is not a significant inhibitor of P-gp.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data on the use of apixaban in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of apixaban during pregnancy.

Breast-feeding

It is unknown whether apixaban or its metabolites are excreted in human milk; available animal data have shown excretion of apixaban in milk. A risk to the breast-fed child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from apixaban therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

Studies in animals dosed with apixaban showed no effect on fertility.

4.7 Effects on ability to drive and use machines

CARDICLEAR 2.5 has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of apixaban has been investigated in four Phase III studies including more than 15,000 patients. The most common adverse reactions were haemorrhage, contusion, epistaxis and haematoma. In the NVAF studies, the overall incidence of bleeding-related adverse reactions was 24.3% (apixaban vs. warfarin) and 9.6% (apixaban vs. acetylsalicylic acid); in the VTEt studies it was 15.6% (vs. enoxaparin/warfarin) and 13.3% (vs. placebo).

Tabulated list of adverse reactions

Adverse reactions are listed below by system organ class, with the frequency for the prevention of stroke and systemic embolism in NVAF and for the treatment/prevention of DVT and PE (VTEt) shown separately. Frequency categories are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from the available data).

System Organ Class / Adverse reaction	NVAF	VTEt
Blood and lymphatic system disorders		
Anaemia	Common	Common
Thrombocytopenia	Uncommon	Common
Immune system disorders		
Hypersensitivity, allergic oedema and anaphylaxis	Uncommon	Uncommon
Pruritus	Uncommon	Uncommon *
Angioedema	Not known	Not known
Nervous system disorders		
Brain haemorrhage †	Uncommon	Rare
Eye disorders		
Eye haemorrhage (including conjunctival haemorrhage)	Common	Uncommon
Vascular disorders		
Haemorrhage, haematoma	Common	Common
Hypotension (including procedural hypotension)	Common	Uncommon
Intra-abdominal haemorrhage	Uncommon	Not known
Respiratory, thoracic and mediastinal disorders		
Epistaxis	Common	Common
Haemoptysis	Uncommon	Uncommon
Respiratory tract haemorrhage	Rare	Rare
Gastrointestinal disorders		
Nausea	Common	Common
Gastrointestinal haemorrhage	Common	Common
Haemorrhoidal haemorrhage	Uncommon	Uncommon
Mouth haemorrhage	Uncommon	Common
Haematochezia	Uncommon	Uncommon
Rectal haemorrhage, gingival bleeding	Common	Common
Retroperitoneal haemorrhage	Rare	Not known
Hepatobiliary disorders		
Liver function test abnormal, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood bilirubin increased	Uncommon	Uncommon
Gamma-glutamyltransferase increased	Common	Common
Alanine aminotransferase increased	Uncommon	Common
Skin and subcutaneous tissue disorders		
Skin rash	Uncommon	Common
Alopecia	Uncommon	Uncommon
Erythema multiforme	Very rare	Not known
Cutaneous vasculitis	Not known	Not known
Musculoskeletal and connective tissue disorders		
Muscle haemorrhage	Rare	Uncommon
Renal and urinary disorders		
Haematuria	Common	Common
Reproductive system and breast disorders		

System Organ Class / Adverse reaction	NVAF	VTEt
Abnormal vaginal haemorrhage, urogenital haemorrhage	Uncommon	Common
General disorders and administration site conditions		
Application site bleeding	Uncommon	Uncommon
Investigations		
Occult blood positive	Uncommon	Uncommon
Injury, poisoning and procedural complications		
Contusion	Common	Common
Post-procedural haemorrhage (including post-procedural haematoma, wound haemorrhage, vessel puncture-site haematoma and catheter-site haemorrhage), wound secretion, incision-site haemorrhage (including incision-site haematoma), operative haemorrhage	Uncommon	Uncommon
Traumatic haemorrhage	Uncommon	Uncommon

* There were no occurrences of generalised pruritus in the long-term VTE-prevention study. † "Brain haemorrhage" encompasses all intracranial or intraspinal haemorrhages (e.g. haemorrhagic stroke, or putamen, cerebellar, intraventricular or subdural haemorrhage).

The use of apixaban may be associated with an increased risk of occult or overt bleeding from any tissue or organ, which may result in post-haemorrhagic anaemia; the signs, symptoms and severity vary according to the location and degree of bleeding.

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 to the National Regulatory Authority.

4.9 Overdose

Overdose of apixaban may result in a higher risk of bleeding. In the event of haemorrhagic complications, treatment must be discontinued and the source of bleeding investigated; appropriate treatment, such as surgical haemostasis or transfusion of fresh frozen plasma, should be considered. The administration of activated charcoal 2 and 6 hours after a 20 mg dose reduced mean apixaban AUC by 50% and 27% respectively, and shortened the half-life; activated charcoal may therefore be useful in the management of apixaban overdose. If life-threatening bleeding cannot be controlled by these measures, administration of prothrombin complex concentrates or recombinant factor VIIa may be considered, and consultation of a coagulation expert should be considered in major bleeding. Haemodialysis is unlikely to be an effective means of managing apixaban overdose.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antithrombotic agents, direct factor Xa inhibitors. ATC code: B01AF02.

Mechanism of action

Apixaban is a potent, oral, reversible, direct and highly selective active-site inhibitor of factor Xa. It does not require antithrombin III for antithrombotic activity and inhibits free and clot-bound factor Xa and prothrombinase activity. Apixaban has no direct effect on platelet aggregation but indirectly inhibits platelet aggregation induced by thrombin. By inhibiting factor Xa, apixaban prevents thrombin generation and thrombus development.

Pharmacodynamic effects

As a result of factor Xa inhibition, apixaban prolongs clotting tests such as prothrombin time (PT), INR and activated partial thromboplastin time (aPTT); changes at the expected therapeutic dose are small and variable and are not recommended for assessing the pharmacodynamic effect. Apixaban demonstrates anti-Factor Xa activity that exhibits a close, approximately linear relationship with plasma concentration, reaching maximum values at peak plasma concentrations.

5.2 Pharmacokinetic properties

Absorption

The absolute bioavailability of apixaban is approximately 50% for doses up to 10 mg. Apixaban is rapidly absorbed, with maximum concentrations 3 to 4 hours after intake, and may be taken with or without food. It displays linear pharmacokinetics with dose-proportional increases in exposure for oral doses up to 10 mg.

Distribution

Plasma protein binding in humans is approximately 87%, and the volume of distribution (Vss) is approximately 21 litres.

Biotransformation and elimination

Apixaban has multiple routes of elimination: about 25% of the dose is recovered as metabolites, mostly in the faeces, and renal excretion accounts for about 27% of total clearance, with additional biliary and direct intestinal excretion. Total clearance is about 3.3 L/h and the half-life is approximately 12 hours. Apixaban is metabolised mainly via CYP3A4/5, with minor contributions from CYP1A2, 2C8, 2C9, 2C19 and 2J2, and is a substrate of P-gp and BCRP; unchanged apixaban is the major circulating component, with no active circulating metabolites.

Special populations

Exposure (AUC) is increased by approximately 16%, 29% and 44% in mild, moderate and severe renal impairment respectively, without an effect on the concentration-anti-Factor Xa relationship. The pharmacokinetics and pharmacodynamics of a single 5 mg dose were not altered in mild or moderate

hepatic impairment. Elderly patients showed approximately 32% higher AUC, exposure was approximately 18% higher in females, and body weight > 120 kg and < 50 kg were associated with approximately 30% lower and 30% higher exposure respectively. No dose adjustment is required on the basis of ethnicity.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential, fertility and embryo-foetal development, and juvenile toxicity. The major effects observed in repeated-dose studies were related to the pharmacodynamic action of apixaban on blood-coagulation parameters; little to no increase in bleeding tendency was found, which should be interpreted with caution when extrapolating to humans owing to the possibly lower sensitivity of the non-clinical species. In rat milk, a high milk-to-maternal-plasma ratio was found, possibly due to active transport into milk.

6. Pharmaceutical particulars

6.1 List of excipients

- Lactose monohydrate
- Sodium lauryl sulphate
- Croscarmellose sodium
- Colloidal silicon dioxide
- Magnesium stearate
- Yellow iron oxide (in the film coating)
- Purified water

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 of children.

6.5 Nature and contents of container

10 tablets in an Alu/PVC blister; three Alu/PVC blisters (30 tablets) packed in a printed carton together with a package insert.

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

UNIZA LIFECARE PRIVATE LIMITED

Sr. No. 919/7 (Old Sr. No. 404), Kadi-Detroj Road, Balasar, Tal: Kadi, Dist: Mehsana, Gujarat, PIN: 382715, India.

8. Marketing Authorisation Number

CTD13082

9. Date of first authorisation / renewal of the authorisation

03.07.2026

10. Date of revision of the text

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