

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cilostazol 100 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg of cilostazol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White to off-white, flat-faced, round tablets, debossed with “100” on one side with an approximate diameter of 8mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cilostazol is indicated for the improvement of the maximal and pain-free walking distances in patients with intermittent claudication, who do not have rest pain and who do not have evidence of peripheral tissue necrosis (peripheral arterial disease Fontaine stage II).

Cilostazol is for second-line use, in patients in whom lifestyle modifications (including stopping smoking and [supervised] exercise programs) and other appropriate interventions have failed to sufficiently improve their intermittent claudication symptoms.

4.2 Posology and method of administration

Posology

The recommended dosage of cilostazol is 100 mg twice a day.

Cilostazol should be initiated by physicians experienced in the management of intermittent claudication (see also section 4.4).

The physician should reassess the patient after 3 months of treatment with a view to discontinuing cilostazol where an inadequate effect is observed or symptoms have not been improved.

Patients receiving treatment with cilostazol should continue with their life-style modifications (smoking cessation and exercise), and pharmacological interventions (such as lipid lowering and antiplatelet treatment) to reduce the risk of cardiovascular events. Cilostazol is not a substitute for such treatments. Reduction of the dose to 50 mg twice daily is recommended in patients receiving medicines that strongly inhibit CYP3A4, for example some macrolides, azole antifungals, protease inhibitors, or medicines that strongly inhibit CYP2C19, for example omeprazole (see sections 4.4 and 4.5).

Older people

There are no special dosage requirements for the elderly.

Paediatric population

The safety and efficacy of cilostazol in children have not been established.

Renal impairment

No dose adjustment is necessary in patients with a creatinine clearance of >25 ml/min. [*Cilostazol*] is contraindicated in patients with a creatinine clearance of ≤ 25 ml/min.

Hepatic impairment

No dosage adjustment is necessary in patients with mild hepatic disease. There are no data in patients with moderate or severe hepatic impairment. Since cilostazol is extensively metabolised by hepatic enzymes, it is contraindicated in patients with moderate or severe hepatic impairment.

Method of administration

For oral use.

Cilostazol should be taken 30 minutes before breakfast and the evening meal. Taking cilostazol with food has been shown to increase the maximum plasma concentrations (C_{max}) of cilostazol, which may be associated with an increased frequency of adverse reactions.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Severe renal impairment: creatinine clearance of ≤ 25 ml/min
- Moderate or severe hepatic impairment
- Congestive heart failure

- Pregnancy
- Patients with any known predisposition to bleeding (e.g. active peptic ulceration, recent (within six months) haemorrhagic stroke, proliferative diabetic retinopathy, poorly controlled hypertension)
- Patients with any history of ventricular tachycardia, ventricular fibrillation or multifocal ventricular ectopics, whether or not adequately treated, and in patients with prolongation of the QTc interval
- Patients with a history of severe tachyarrhythmia
- Patients treated concomitantly with two or more additional antiplatelet or anticoagulant agents (e.g. acetylsalicylic acid, clopidogrel, heparin, warfarin, acenocoumarol, dabigatran, rivaroxaban or apixaban)
- Patients with unstable angina pectoris, myocardial infarction within the last 6 months, or a coronary intervention in the last 6 months.

4.4 Special warnings and precautions for use

The suitability of treatment with cilostazol should be carefully considered alongside other treatment options such as revascularisation.

Based on its mechanism of action, cilostazol may induce tachycardia, palpitation, tachyarrhythmia and/or hypotension. The increase in heart rate associated with cilostazol is approximately 5 to 7 bpm; in patients at risk this consequently may induce angina pectoris.

Patients who may be at increased risk for serious cardiac adverse events as a result of increased heart rate, e.g. patients with stable coronary disease, should be closely monitored during treatment with cilostazol, while the use of cilostazol in patients with unstable angina pectoris, or myocardial infarction/coronary intervention within the last 6 months, or a history of severe tachyarrhythmia is contraindicated (see section 4.3).

Caution should be exercised when prescribing cilostazol for patients with atrial or ventricular ectopy and patients with atrial fibrillation or flutter.

Patients should be warned to report any episode of bleeding or easy bruising whilst on therapy. In case of retinal bleeding administration of cilostazol should be stopped. Refer to sections 4.3 and 4.5 for further information on bleeding risks.

Due to cilostazol's platelet aggregation inhibitory effect it is possible that an increased bleeding risk occurs in combination with surgery (including minor invasive measurements like tooth extraction). If a patient is to undergo elective surgery and antiplatelet effect is not necessary, cilostazol should be stopped 5 days prior to surgery.

There have been rare or very rare reports of haematological abnormalities including thrombocytopenia, leucopenia, agranulocytosis, pancytopenia and aplastic anaemia (see section 4.8). Most patients recovered on discontinuation of cilostazol. However, some cases of pancytopenia and aplastic anaemia had a fatal outcome.

In addition to reporting episodes of bleeding and easy bruising, patients should be warned to promptly report any other signs which might also suggest the early development of blood dyscrasia such as pyrexia and sore throat. A full blood count should be performed if infection is suspected or there is any other clinical evidence of blood dyscrasia. Cilostazol should be discontinued promptly if there is clinical or laboratory evidence of haematological abnormalities.

In the case of patients receiving strong inhibitors for CYP3A4 or CYP2C19, plasma levels of cilostazol were shown to be increased. In such cases, a cilostazol dosage of 50 mg twice daily is recommended (see section 4.5 for further information).

Caution is needed when co-administering cilostazol with any other agent which has the potential to reduce blood pressure due to the possibility that there may be an additive hypotensive effect with a reflex tachycardia. Refer also to section 4.8.

Caution should be exercised when co-administering cilostazol with any other agents that inhibit platelet aggregation. Refer to sections 4.3 and 4.5.

4.5 Interaction with other medicinal products and other forms of interaction

Inhibitors of platelet aggregation

Cilostazol is a PDE III inhibitor with antiplatelet activity. In a clinical study in healthy subjects, cilostazol given 150mg b.i.d. for five days did not result in prolongation of bleeding time.

Acetylsalicylic Acid (ASA)

Short term (≤ 4 days) co-administration of ASA with cilostazol suggested a 23-25% increase in inhibition of ADP-induced *ex vivo* platelet aggregation when compared to ASA alone.

There were no apparent trends toward a greater frequency of haemorrhagic adverse effects in patients taking cilostazol and ASA compared to patients taking placebo and equivalent doses of ASA.

Clopidogrel and other antiplatelet drugs

Concomitant administration of cilostazol and clopidogrel did not have any effect on platelet count, prothrombin time (PT) or activated partial thromboplastin time (aPTT). All healthy subjects in the study had a prolongation of bleeding time on clopidogrel alone and concomitant administration with cilostazol did not result in a significant additional effect on bleeding time. Caution is advised when co-administering cilostazol with any drug that inhibits platelet aggregation. Consideration should be given to monitoring the bleeding time at intervals. Cilostazol treatment is contraindicated in patients receiving two or more additional antiplatelet/anticoagulant agents (see section 4.3).

A higher rate of haemorrhage was observed with the concomitant use of clopidogrel, ASA and cilostazol in the CASTLE trial.

Oral Anticoagulants like warfarin

In a single-dose clinical study, no inhibition of the metabolism of warfarin or an effect on the coagulation parameters (PT, aPTT, bleeding time) was observed. However, caution is advised in patients receiving both cilostazol and any anticoagulant agent, and frequent monitoring is required to reduce the possibility of bleeding.

Cilostazol treatment is contraindicated in patients receiving two or more additional antiplatelet/anticoagulant agents (see section 4.3).

Cytochrome P-450 (CYP) enzyme inhibitors

Cilostazol is extensively metabolised by CYP enzymes, particularly CYP3A4 and CYP2C19 and to a lesser extent CYP1A2. The dehydro metabolite, which has 4-7 times the potency of cilostazol in inhibiting platelet aggregation, appears to be formed primarily via CYP3A4. The 4'-trans-hydroxy metabolite, with potency one-fifth that of cilostazol, appears to be formed primarily via CYP2C19. Therefore, drugs inhibiting CYP3A4 (e.g., some macrolides, azole antifungals, protease inhibitors) or CYP2C19 (like proton pump inhibitors, PPIs) increase the total pharmacological activity and could have the potential to enhance the undesirable effects of cilostazol. Consequently, for patients concomitantly taking strong CYP3A4 or CYP2C19 inhibitors the recommended dose is 50 mg twice daily (see section 4.2).

Administration of cilostazol with erythromycin (an inhibitor of CYP3A4) resulted in an increase in the AUC of cilostazol by 72%, accompanied by a 6% increase in AUC of the dehydro metabolite and a 119% increase in AUC of the 4'-trans-hydroxy metabolite.

Based on AUC, the overall pharmacological activity of cilostazol increases 34% when co-administered with erythromycin. Based on these data, the recommended dose of cilostazol is 50 mg bid in the presence of erythromycin and similar agents (e.g., clarithromycin).

Co-administration of ketoconazole (an inhibitor of CYP3A4 with cilostazol) resulted in a 117% increase in the AUC of cilostazol, accompanied by a 15% decrease in the AUC of the dehydro metabolite and a 87% increase in the AUC of the 4'-trans-hydroxy metabolite. Based on AUC, the overall pharmacological activity of cilostazol increases 35% when co-administered with ketoconazole. Based on these data, the recommended dose of cilostazol is 50 mg bid in the presence of ketoconazole and similar agents (e.g., itraconazole).

Administration of cilostazol with diltiazem (a weak inhibitor of CYP3A4) resulted in an increase in the AUC of cilostazol of 44%, accompanied by a 4% increase in AUC of the dehydro metabolite and a 43% increase in the AUC of the 4'-trans-hydroxy metabolite.

Based on AUC, overall pharmacological activity of cilostazol increases 19% when co-administered with diltiazem. Based on these data, no dose adjustment is necessary.

Administration of a single dose of 100 mg cilostazol with 240 ml grapefruit juice (an inhibitor of intestinal CYP3A4) did not have a notable effect on the pharmacokinetics of cilostazol. Based on these data, no dose adjustment is necessary. A clinically relevant effect on cilostazol is still possible at higher quantities of grapefruit juice.

Administration of cilostazol with omeprazole (an inhibitor of CYP2C19) increased the AUC of cilostazol by 22%, accompanied by a 68% increase in the AUC of the dehydro metabolite and a decrease of 36% in the AUC of the 4'-trans hydroxy metabolite. Based on AUC, the overall pharmacological activity increases by 47% when co-administered with omeprazole. Based on these data, the recommended dose of cilostazol is 50 mg bid in the presence of omeprazole.

Cytochrome P-450 enzyme substrates

Cilostazol has been shown to increase the AUC of lovastatin (sensitive substrate for CYP3A4) and its β -hydroxy acid by 70%. Caution is advised when cilostazol is co-administered with CYP3A4 substrates with a narrow therapeutic index (e.g., cisapride, halofantrine, pimozide, ergot derivatives). Caution is advised in case of co-administration with statins metabolised by CYP3A4, for example simvastatin, atorvastatin and lovastatin.

Cytochrome P-450 enzyme inducers

The effect of CYP3A4 and CYP2C19 inducers (such as carbamazepine, phenytoin, rifampicin and St. John's wort) on cilostazol pharmacokinetics has not been evaluated. The antiplatelet effect may theoretically be altered and should be carefully monitored when cilostazol is co-administered with CYP3A4 and CYP2C19 inducers.

In clinical trials, smoking (which induces CYP1A2) decreased cilostazol plasma concentrations by 18%.

Other potential interactions

Caution is needed when co-administering cilostazol with any other agent which has the potential to reduce blood pressure due to the possibility that there may be an additive hypotensive effect with a reflex tachycardia.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data in the use of cilostazol in pregnant women. Studies in animals have shown reproductive toxicity (see Section 5.3). The potential risk for humans is unknown. Cilostazol must not be used during pregnancy (see section 4.3).

Breast-feeding

The transfer of cilostazol to breast milk has been reported in animal studies. The excretion of cilostazol in human milk is unknown. Due to the potential harmful effect in the newborn child breast fed by a treated mother, the use of cilostazol is not recommended during breast feeding.

Fertility

Cilostazol reversibly impaired fertility of female mice but not in other animal species (see section 5.3). The clinical significance is unknown.

4.7 Effects on ability to drive and use machines

Cilostazol may cause dizziness and patients should be warned to exercise caution before they drive or operate machinery.

4.8 Undesirable effects

The most commonly reported adverse reactions in clinical trials were headache (in >30%), diarrhoea and abnormal stools (in >15% each). These reactions were usually of mild to moderate intensity and were sometimes alleviated by reducing the dose.

Adverse reactions reported in clinical trials and in the post-marketing period are included in the table below.

	Very common ($\geq 1/10$)	Common ($\geq 1/100$ to <1/10)	Uncommon ($\geq 1/1,000$ to <1/100)	Rare ($\geq 1/10,000$ to <1/1,000)	Very rare (<1/10,000)	Not known (cannot be estimated from the \geq available data)
<i>Blood and lymphatic system disorders</i>		Ecchymosis	Anaemia	Bleeding time prolonged, thrombocytopenia		Bleeding tendency, thrombocytopenia, granulocytopenia, agranulocytosis, leukopenia, pancytopenia, aplastic anaemia
<i>Immune system disorders</i>			Allergic reaction			
<i>Metabolism and nutrition disorders</i>		Oedema (peripheral, face), anorexia	Hyperglycaemia, Diabetes mellitus			
<i>Psychiatric disorders</i>			Anxiety			
<i>Nervous system disorders</i>	Headache	Dizziness	Insomnia, abnormal dreams			Paresis, hypoesthesia
<i>Eye disorders</i>						Conjunctivitis
<i>Ear and labyrinth</i>						Tinnitus

<i>disorders</i>						
<i>Cardiac disorders</i>		Palpitation, tachycardia, angina pectoris, arrhythmia, ventricular extrasystoles	Myocardial infarction, atrial fibrillation, congestive heart failure, supraventricular tachycardia, ventricular tachycardia, syncope			
<i>Vascular disorders</i>			Eye haemorrhage, epistaxis, gastrointestinal haemorrhage, haemorrhage unspecified, orthostatic hypotension			Hot flushes, hypertension, hypotension, cerebral haemorrhage, pulmonary haemorrhage, muscle haemorrhage, respiratory tract haemorrhage, subcutaneous haemorrhage
<i>Respiratory, thoracic and mediastinal disorders</i>		Rhinitis, pharyngitis	Dyspnoea, pneumonia, cough			Interstitial pneumonia
<i>Gastrointestinal disorders</i>	Diarrhoea, abnormal faeces	Nausea and vomiting, dyspepsia, flatulence, abdominal pain	Gastritis			
<i>Hepatobiliary disorders</i>						Hepatitis, hepatic function abnormal, jaundice
<i>Skin and subcutaneous tissue disorders</i>		Rash, pruritus				Eczema, skin eruptions, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria

<i>Musculoskeletal and connective tissue disorders</i>			Myalgia			
<i>Renal and urinary disorders</i>				Renal failure, renal impairment		Haematuria, pollakiuria
<i>General disorders and administration site conditions</i>		Chest pain, asthenia	Chills, malaise			Pyrexia, pain
<i>Investigations</i>						Uric acid level increased, blood urea increased, blood creatinine increased

An increase in the frequency of palpitation and peripheral oedema was observed when cilostazol was combined with other vasodilators that cause reflex tachycardia e.g. dihydropyridine calcium channel blockers.

The only adverse event resulting in discontinuation of therapy in $\geq 3\%$ of patients treated with cilostazol was headache. Other frequent causes of discontinuation included palpitation and diarrhoea (both 1.1%).

Cilostazol *per se* may carry an increased risk of bleeding and this risk may be potentiated by co administration with any other agent with such potential.

The risk of intraocular bleeding may be higher in patients with diabetes.

An increase in the frequency of diarrhoea and palpitation has been found in patients older than 70 years.

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google play or Apple App Store.

4.9 Overdose

Information on acute overdose in humans is limited. The signs and symptoms can be anticipated to be severe headache, diarrhoea, tachycardia and possibly cardiac arrhythmias.

Patients should be observed and given supportive treatment. The stomach should be emptied by induced vomiting or gastric lavage, as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antithrombotic agents, platelet aggregation inhibitor excl. heparin,
ATC code: B01AC23

Mechanism of action

Cilostazol and several of its metabolites are phosphodiesterase III inhibitors which suppress cyclic AMP degradation, resulting in increased cAMP in a variety of tissues including platelets and blood vessels

Pharmacodynamic effects

From data generated in nine placebo-controlled studies (where 1,634 patients were exposed to cilostazol), it has been demonstrated that cilostazol improves exercise capacity as judged by changes in Absolute Claudication Distance (ACD, or maximal walking distance) and Initial Claudication Distance (ICD, or pain-free walking distance) upon treadmill testing. Following 24 weeks treatment, cilostazol 100 mg b.i.d. increases in mean ACD ranged from 60.4 - 129.1 metres, whilst mean ICD increases ranged from 47.3 - 93.6 metres.

A meta-analysis based on weighted mean differences across the nine studies indicated that there was a significant absolute overall post-baseline improvement of 42 m in maximal walking distance (ACD) for cilostazol 100 mg b.i.d. over the improvement seen under placebo. This corresponds to a relative improvement of 100% over placebo. This effect appeared lower in diabetics than in non-diabetics.

Animal studies have shown cilostazol to have vasodilator effects and this has been demonstrated in small studies in man where ankle blood flow was measured by strain gauge plethysmography. cilostazol also inhibits smooth muscle cell proliferation in rat and human smooth muscle cells *in vitro*, and inhibits the platelet release reaction of platelet-derived growth factor and PF-4 in human platelets.

Studies in animals and in man (*in vivo* and *ex vivo*) have shown that cilostazol causes reversible inhibition of platelet aggregation. The inhibition is effective against a range of aggregants (including shear stress, arachidonic acid, collagen, ADP and adrenaline); in man the inhibition lasts for up to 12 hours, and on cessation of administration of cilostazol recovery of aggregation

occurred within 48-96 hours, without rebound hyperaggregability. Effects on circulating plasma lipids have been examined in patients taking cilostazol. After 12 weeks, as compared to placebo, cilostazol 100 mg b.i.d. produced a reduction in triglycerides of 0.33 mmol/l (15%) and an increase in HDL-cholesterol of 0.10 mmol/l (10%).

Clinical efficacy and safety

A randomized, double-blind, placebo-controlled Phase IV study was conducted to assess the long-term effects of cilostazol, with focus on mortality and safety. In total, 1,439 patients with intermittent claudication and no heart failure have been treated with cilostazol or placebo for up to three years. With respect to mortality, the observed 36-month Kaplan-Meier event rate for deaths on study drug with a median time on study drug of 18 months was 5.6% (95% CI of 2.8 to 8.4%) on cilostazol and 6.8% (95% CI of 1.9 to 11.5%) on placebo. Long-term treatment with cilostazol did not raise safety concerns.

5.2 Pharmacokinetic properties

Following multiple doses of cilostazol 100 mg twice daily in patients with peripheral vascular disease, steady state is achieved within 4 days.

Absorption

The C_{max} of cilostazol and its primary circulating metabolites increase less than proportionally with increasing doses. However, the AUC for cilostazol and its metabolites increase approximately proportionately with dose.

Distribution

Cilostazol is 95-98% protein bound, predominantly to albumin. The dehydro metabolite and 4'-trans-hydroxy metabolite are 97.4% and 66% protein bound respectively.

Biotransformation

The apparent elimination half-life of cilostazol is 10.5 hours. There are two major metabolites, a dehydro-cilostazol and a 4'-trans-hydroxy cilostazol, both of which have similar apparent half-lives. The dehydro metabolite is 4-7 times as active a platelet antiaggregant as the parent compound and the 4'-trans-hydroxymetabolite is one fifth as active. Plasma concentrations (as measured by AUC) of the dehydro and 4'-trans-hydroxy metabolites are ~41% and ~12% of cilostazol concentrations.

Cilostazol is eliminated predominantly by metabolism and subsequent urinary excretion of metabolites. The primary isoenzymes involved in its metabolism are cytochrome P-450 CYP3A4, to a lesser extent, CYP2C19, and to an even lesser extent CYP1A2.

Elimination

The primary route of elimination is urinary (74%) with the remainder excreted in the faeces. No measurable amount of unchanged cilostazol is excreted in the urine, and less than 2% of the dose is excreted as the dehydro-cilostazol

metabolite. Approximately 30% of the dose is excreted in the urine as the 4'-trans-hydroxy metabolite. The remainder is excreted as metabolites, none of which exceed 5% of the total excreted.

There is no evidence that cilostazol induces hepatic microsomal enzymes.

Older people

The pharmacokinetics of cilostazol and its metabolites were not significantly affected by age or gender in healthy subjects aged between 50-80 years.

In subjects with severe renal impairment, the free fraction of cilostazol was 27% higher and both C_{max} and AUC were 29% and 39% lower respectively than in subjects with normal renal function. The C_{max} and AUC of the dehydro metabolite were 41% and 47% lower respectively in the severely renally impaired subjects compared to subjects with normal renal function. The C_{max} and AUC of 4'-trans-hydroxy cilostazol were 173% and 209% greater in subjects with severe renal impairment. The medicine must not be administered to patients with a creatinine clearance <25ml/min (see section 4.3).

Hepatic impairment

There are no data in patients with moderate to severe hepatic impairment and since cilostazol is extensively metabolised by hepatic enzymes, the medicine must not be used in such patients (see section 4.3).

5.3 Preclinical safety data

As with other positive inotropic and vasodilator agents, cilostazol produced cardiovascular lesions in dogs. Such lesions were not seen in rats or monkeys and are considered species specific. Investigation of QTc in dogs and monkeys showed no prolongation after administration of cilostazol or its metabolites.

Mutagenicity studies were negative in bacterial gene mutation, bacterial DNA repair, mammalian cell gene mutation and mouse *in vivo* bone marrow chromosomal aberrations. In *in vitro* tests on Chinese ovary hamster cells cilostazol produced a weak but significant increase in chromosome aberration frequency. No unusual neoplastic outcomes were observed in two-year carcinogenicity studies in rats at oral (dietary) doses up to 500 mg/kg/day, and in mice at doses up to 1000 mg/kg/day.

In rats dosed during pregnancy, foetal weights were decreased. In addition, an increase in fetuses with external, visceral and skeletal abnormalities was noted at high dose levels. At lower dose levels, retardations of ossification were observed. Exposure in late pregnancy resulted in an increased frequency of stillbirths and lower offspring weights. An increased frequency of retardation of ossification of the sternum was observed in rabbits.

Cilostazol inhibited mouse oocyte maturation *in vitro*, and in female mice caused a reversible impairment of fertility. No effect on fertility was observed in rats or in non-human primates. The relevance to humans is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Cellulose, microcrystalline
Carmellose calcium
Hypromellose
Magnesium stearate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Cartons containing 7, 10, 14 and 56 tablets packed in PVC/PVDC Aluminium blisters.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Generics [UK] Limited t/a Viatrix
Station Close,
Potters Bar,
Hertfordshire,
EN6 1TL,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 04569/1427

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
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23/02/2015

10 DATE OF REVISION OF THE TEXT

15/05/2026