SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aceclofenac 100 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 100 mg of aceclofenac

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White, round, biconvex film-coated tablets, 8 mm diameter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Aceclofenac 100 mg Film-coated Tablets is indicated for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in adults.

4.2 Posology and method of administration

Posology

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

Adults

The recommended dose is 200 mg daily, taken as two separate 100 mg doses, one tablet in the morning and one in the evening.

Children

There are no clinical data on the use of Aceclofenac 100 mg Tablets in children and therefore it is not recommended for use in children.

Elderly

The elderly, who are more likely to be suffering from impaired renal, cardiovascular or hepatic function and receiving concomitant medication, are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

The pharmacokinetics of Aceclofenac 100 mg Tablets are not altered in elderly patients, therefore it is not considered necessary to modify the dose or dose frequency.

Patients with renal impairment

There is no evidence that the dosage of Aceclofenac 100 mg Tablets needs to be modified in patients with mild renal impairment, but as with other NSAIDs caution should be exercised (see section4.4).

Patients with liver impairment

There is some evidence that the dose of Aceclofenac 100 mg Tablets should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of 100 mg be used.

Method of administration

Aceclofenac 100 mg Film-coated Tablets are supplied for oral administration and should be swallowed whole with a sufficient quantity of liquid.

To be taken preferably with or after food. When Aceclofenac 100 mg Tablets was administered to fasting and fed healthy volunteers only the rate and not the extent of aceclofenac absorption was affected

4.3 Contraindications

Hypersensitivity to aceclofenac or to any of the excipients listed in section 6.1

Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.

Patients with active bleeding or bleeding diathesis.

Severe hepatic failure and renal failure (see section 4.4).

Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Aceclofenac 100 mg Tablets should not be prescribed during pregnancy, especially during the last trimester of pregnancy, in women attempting to conceive and lactation unless there are compelling reasons for doing so. The lowest effective dosage should be used (see section 4.6).

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below).

The use of Aceclofenac 100 mg Tablets with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Elderly:

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2).

Respiratory disorders:

Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

Cardiovascular, Renal and Hepatic Impairment:

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients (see also section 4.3).

Renal:

Patients with mild to moderate renal impairment should be kept under surveillance, since the use of NSAIDs may result in deterioration of renal function. The lowest effective dose should be used and renal function

monitored regularly. Effects on renal function are usually reversible on withdrawal of Aceclofenac 100 mg Tablets.

Hepatic:

If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), Aceclofenac 100 mg Tablets should be discontinued. Close medical surveillance is necessary in patients suffering from mild to moderate impairment of hepatic function. Hepatitis may occur without prodromal symptoms.

Use of Aceclofenac 100 mg Tablets in patients with hepatic porphyria may trigger an attack.

Cardiovascular and cerebrovascular effects:

Patients with congestive heart failure (NYHA-I) and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with aceclofenac after careful consideration.

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild congestive heart failure (NYHA-I) as fluid retention and oedema have been reported in association with NSAID therapy.

As the cardiovascular risks of aceclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient’s need for symptomatic relief and response to therapy should be re-evaluated periodically.

Aceclofenac should also be administered with caution and under close medical surveillance to patients with a history of cerebrovascular bleeding

Gastrointestinal bleeding, ulceration and perforation:

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

Close medical surveillance is imperative in patients with symptoms indicative of gastro-intestinal disorders involving either the upper or lower gastrointestinal tract, with a history suggestive of gastro-intestinal ulceration, with ulcerative colitis or with Crohn's disease, bleeding diathesis or perforation, or haematological abnormalities, as these conditions may be exacerbated (see section 4.8).

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated

with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving aceclofenac, the treatment should be withdrawn.

SLE and mixed connective tissue disease:

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

Dermatological:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Aceclofenac 100 mg Film-coated Tablets should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Exceptionally, varicella can trigger serious cutaneous and soft tissues infections complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of aceclofenac in case of varicella.

Impaired female fertility:

The use of Aceclofenac 100 mg Tablets may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Aceclofenac 100 mg Film-coated Tablets should be considered.

Hypersensitivity reactions:

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

Haematological:

Aceclofenac 100 mg Tablets may reversibly inhibit platelet aggregation (see section 4.5 anticoagulants under 'Interactions').

Aceclofenac should be avoided in patients who have developed anaemia, agranulocytosis or thrombocytopenia secondary to NSAIDs or metamizol.

Long term treatment:

All patients who are receiving NSAIDs should be monitored as a precautionary measure e.g. renal failure, hepatic function (elevation of liver enzymes may occur) and blood counts.

4.5 Interaction with other medicinal products and other forms of interaction

Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects, including GI bleeding (see section 4.4).
Anti-hypertensives: Reduced anti-hypertensive effect. The risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients or elderly patients) when ACE- inhibitors or angiotensin II receptor antagonists are combined with NSAIDs. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs. Although it was not shown to affect blood pressure control when co-administered with bendrofluazide, interactions with other diuretics cannot be ruled out. When concomitant administration with potassium-sparing diuretics is employed, serum potassium should be monitored.

Cardiac glycosides like digoxin:: NSAIDs may exacerbate cardiac failure, reduce GFR (glomerular filtration rate) and increase plasma glycoside levels. The combination should be avoided unless frequent monitoring of glycoside levels can be performed.
Lithium: Several NSAIDs drugs inhibit the renal clearance of lithium, resulting in increased serum concentration of lithium. The combination should be avoided unless frequent monitoring of lithium can be performed.

Methotrexate: The possible interaction between NSAIDs and methotrexate should be born in mind also when low doses of methotrexate are used, especially in patients with decreased renal function. When combination therapy has to be used, the renal function should be monitored. Caution should be exercised if NSAIDs and methotrexate are administered within 24 hours of each other, since NSAIDs may increase plasma levels, resulting in increased toxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4). Close monitoring of patients on combined anti-coagulants and Aceclofenac 100 mg Film-coated Tablets therapy should be undertaken.

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).
Ciclosporin,tacrolimus: Administration of NSAID drugs together with cyclosporin or tacrolimus is thought to increase the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney. During combination therapy it is therefore important to carefully monitor renal function.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Antidiabetic agents: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of hypoglycaemic and hyperglycaemic effects. Thus with Aceclofenac 100 mg Film-coated Tablets, consideration should be given to adjustment of the dosage of hypoglycaemic agents.

Other NSAIDs: Concomitant therapy with aspirin or other NSAIDs may increase the frequency of adverse reactions, including the risk of GI bleeding.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There is no information on the use of aceclofenac during pregnancy. Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation or gastroschisis after use of prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. From the 20th week of pregnancy onward, aceclofenac use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, aceclofenac should not be given unless clearly necessary. If aceclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to aceclofenac for several days from gestational week 20 onward. Aceclofenac should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);

- renal dysfunction (see above)-, which may progress to renal failure with oligo-hydroamniosis;

the mother and the neonate, at the end of pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.

- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, aceclofenac is contraindicated during the third trimester of pregnancy (see section 4.3).

Lactation

There is no information on the secretion of aceclofenac to breast milk; there was however no notable transfer of radio labelled (14C) aceclofenac to the milk of lactating rats.

The use of aceclofenac should therefore be avoided in pregnancy and lactation unless the potential benefits to the other outweigh the possible risks to the foetus.

Fertility

The use of aceclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Aceclofenac 100 mg Film-coated Tablets should be considered.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances or other central nervous system disorders are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Gastrointestinal: The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (See section 4.4) have been reported following administration. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Cardiovascular and cerebrovascular: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.
Aceclofenac is both structurally related and metabolised to diclofenac for which a greater amount of clinical and epidemiological data consistently point towards an increased risk of general arterial thrombotic events (myocardial infarction or stroke, particularly at high doses and in long treatment). Epidemiological data has also found an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac, (see section 4.3 and 4.4).

Exceptionally, occurrence of serious cutaneous and soft tissues infections complications during varicella has been reported in association with NSAID treatment.

Other adverse reactions reported less commonly include:

Renal: Interstitial nephritis.

Hepatic: abnormal liver function, hepatitis and jaundice.

Neurological and special senses: Optic neuritis, reports of aseptic meningitis (especially in patients with existing auto immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (See section 4.4), confusion, hallucinations, and drowsiness.

Haematological: Agranulocytosis, aplastic anaemia.

Dermatological: Bullous reactions including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (very rare). Photosensitivity.

If serious adverse reactions occur, Aceclofenac 100 mg film-coated Tablets should be withdrawn.

Within the system organ classes, undesirable effects are listed under headings of frequency, using the following categories: 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), not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System organ class	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Very rare/ isolated reports (<1/10,000)**
Blood and lymphatic			Anaemia	Bone Marrow

system disorders				depression Granulocytopenia Thrombocytopenia Neutropenia Haemolytic anaemia
Immune system disorders			Anaphylactic reaction (including shock) Hypersensitivity	
Metabolism and nutrition disorders				Hyperkalemia
Psychiatric disorders				Depression Abnormal dreams Insomnia
Nervous system disorders	Dizziness			Paraesthesia Tremor Somnolence Headache Dysgeusia (abnormal taste)
Eye disorders			Visual disturbance	
Ear and labyrinth disorders				Vertigo Tinnitus

Cardiac disorders			Cardiac failure	Palpitations
Vascular disorders			Hypertension	Flushing Hot flush Vasculitis
Respiratory, thoracic and mediastinal disorders			Dyspnoea	Bronchospasm Stridor
Gastrointestinal disorders	Dyspepsia Abdominal pain Nausea Diarrhoea	Flatulence Gastritis Constipation Vomiting Mouth ulceration	Melaena Gastrointestinal haemorrhage Gastrointestinal ulceration	Stomatitis Intestinal perforation Exacerbation of Crohn's disease and Colitis Ulcerative Haematemesis Pancreatitis
Hepatobiliary disorders	Hepatic enzyme increased			Hepatic injury (including hepatitis) Jaundice Blood alkaline phosphatase increased
Skin and subcutaneous tissue disorders		Pruritus Rash Dermatitis Urticaria	Angioedema	Purpura Severe mucocutaneous skin reaction (including Stevens Johnson Syndrome and

				Toxic Epidermal Necrolysis)
Renal and urinary disorders		Blood urea increased Blood creatinine increased		Renal failure Nephrotic syndrome
General disorders and administration site conditions				Oedema Fatigue Cramps in legs
Investigations				Weight increase

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal products. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Management of acute poisoning with NSAIDs essentially consists of supportive and symptomatic measures.

a) Symptoms

Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal irritation, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, hypotension, respiratory depression, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

b) Therapeutic measure

Patients should be treated symptomatically as required.

Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Specific therapies such as dialysis or haemoperfusion are probable of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

In case of frequent or prolonged convulsions, patients should be treated with intravenous diazepam.

Other measures may be indicated by the patient's clinical condition.

Management of acute poisoning with oral aceclofenac essentially consists of supportive and symptomatic measures for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinflammatory and antirheumatic products, non-steroids, acetic acid derivatives and related substances

ATC code: M01AB16.

Aceclofenac is a non-steroidal agent with marked anti-inflammatory and analgesic properties.

The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

5.2 Pharmacokinetic properties

After oral administration, aceclofenac is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hours following ingestion. Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 57% of those in plasma. The volume of distribution is approximately 25 L.

The mean plasma elimination half-life is around 4 hours. Aceclofenac is highly protein- bound (>99%). Aceclofenac circulates mainly as unchanged drug. 4'- Hydroxyaceclofenac is the main metabolite detected in plasma. Approximately two- thirds of the administered dose is excreted via the urine, mainly as hydroxymetabolites.

Aceclofenac is partially metabolised to diclofenac.

No changes in the pharmacokinetics of aceclofenac have been detected in the elderly.

5.3 Preclinical safety data

The results from preclinical studies conducted with aceclofenac are consistent with those expected for NSAIDs. The principal target organ was the gastro-intestinal tract. No unexpected findings were recorded.

Aceclofenac was not considered to have any mutagenic activity in three *in vitro* studies and an *in vivo* study in the mouse.

Aceclofenac was not found to be carcinogenic in either the mouse or rat.

Animal studies indicate that there was no evidence of teratogenesis in rats although the systemic exposure was low and in rabbits treatment with aceclofenac (10 mg/kg/day) resulted in a series of morphological changes in some fetuses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:

Microcrystalline cellulose (E460i)

Croscarmellose Sodium

Copovidone

Talc (E553b)
Silica colloidal anhydrous
Glicerol distearate

Film-coating Opadry O3A0280002:
HPMC 2910/Hypromellose
Microcrystalline Cellulose
Titanium dioxide (E171)
Polyoxyl 40 (Macrogol)stearate

6.2 Incompatibilities

None known

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

Aceclofenac 100 mg Film-Coated Tablets are packaged in Aluminium/aluminium blisters placed into cardboard boxes containing 20, 30, 40, 60, 90, 100 or 180 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

RIVOPHARM UK Ltd.
100 Bishopsgate
London
EC2N 4AG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 33155/0029

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/11/2025

10 DATE OF REVISION OF THE TEXT

05/11/2025