Professional Information for KETESSE

SCHEDULING STATUS: S3

1. NAME OF THE MEDICINE

KETESSE 25 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25 mg dexketoprofen (as dexketoprofen trometamol).

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

White film-coated tablets, scored on both sides, with convex sides.

The tablets can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic short-term treatment of pain of mild to moderate intensity, such as musculoskeletal pain, dysmenorrhoea, dental pain.

4.2 Posology and method of administration

Posology

Adults

According to the nature and severity of pain, the recommended dosage is 12,5 mg every 4 – 6 hours or 25 mg every 8 hours. The total daily dose should not exceed 75 mg.

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

KETESSE are not intended for long-term use and the treatment must be limited to the symptomatic period.

Elderly patients

In elderly patients it is recommended to start the therapy at the lower end of the dosage range (50 mg total daily dose). The dosage may be increased to that recommended for the general population only after good general tolerance has been ascertained.

Hepatic impairment

Patients with mild to moderate hepatic dysfunction should start therapy at reduced doses (50 mg total daily dose) and be closely monitored. KETESSE should not be used in patients with severe hepatic dysfunction (see section 4.3).

Renal impairment

The initial dosage should be reduced to 50 mg total daily dose in patients with mildly impaired renal function (creatinine clearance 60 – 89 mL/min) (see section 4.4). KETESSE should not be used in patients with moderate to severe renal dysfunction (creatinine clearance ≤ 59 mL/min) (see section 4.3).

Paediatric population

KETESSE has not been studied in children and adolescents. Therefore, the safety and efficacy in children and adolescents have not been established and KETESSE should not be used in children and adolescents.

Method of administration

The tablet should be swallowed with a sufficient amount of fluid (e.g. one glass of water). Concomitant administration with food delays the absorption rate of the medicine (see section 5.2), thus in case of acute pain it is recommended that administration is at least 30 minutes before meals.

4.3 Contraindications

KETESSE must not be administered in the following cases:

- Patients hypersensitive to dexketoprofen trometamol, to any other nonsteroidal antiinflammatory (NSAIDs), or to any of the excipients listed in section 6.1.
- Patients in whom substances with a similar action (e.g. acetylsalicylic acid, or other NSAIDs) precipitate attacks of asthma, bronchospasm, acute rhinitis, or cause nasal polyps, urticaria or angioneurotic oedema.
- Known photoallergic or phototoxic reactions during treatment with ketoprofen or fibrates.
- Patients with history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Patients with active peptic ulcer/gastrointestinal haemorrhage or any history of gastrointestinal bleeding, ulceration or perforation.
- Patients with chronic dyspepsia.
- Patients who have other active bleedings or bleeding disorders.
- Patients with Crohn's disease or ulcerative colitis.
- Patients with severe heart failure.
- Patients with moderate to severe renal dysfunction (creatinine clearance ≤ 59 mL/min).
- Patients with severely impaired hepatic function (Child-Pugh score 10 – 15).
- Patients with haemorrhagic diathesis and other coagulation disorders.
- Patients with severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).
- Pregnancy and lactation (see section 4.6).
- Congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria).

4.4 Special warnings and precautions for use

Administer with caution in patients with a history of allergic conditions.

KETESSE should not be used concomitantly with other NSAIDs including cyclooxygenase-2 (COX-2) selective inhibitors (see section 4.5).

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).

Gastrointestinal safety

Gastrointestinal bleeding, ulceration or perforation which can be fatal, have been reported with NSAIDs, such as KETESSE, at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events. When gastrointestinal bleeding or ulceration occurs in patients receiving KETESSE, the treatment should be withdrawn.

Elderly patients: The elderly has an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation, which may be fatal (see section 4.2). These patients should commence treatment on the lowest dose available.

Any history of oesophagitis, gastritis and/or peptic ulcer must be sought in order to ensure their total cure before starting treatment with KETESSE. Patients with gastrointestinal symptoms or history of gastrointestinal disease should be monitored for digestive disturbances, especially gastrointestinal bleeding.

KETESSE, should be given with care to patients with a history of gastrointestinal disease as their condition may be exacerbated (see section 4.8).

Combination therapy with protective medicines (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid, or other medicines likely to increase gastrointestinal risk (see below and section 4.5).

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

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

Renal safety

Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of NSAIDs at higher than recommended doses (see sections 4.8 and 4.9). Presenting signs and symptoms included reduced level of consciousness and generalised weakness. NSAID-induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

Caution should be exercised in patients with impairment of renal functions. In these patients, KETESSE may result in deterioration of renal function, fluid retention and oedema. Caution is also required in patients receiving diuretic therapy or those who could develop hypovolaemia as there is an increased risk of nephrotoxicity.
Adequate fluid intake should be ensured during treatment to prevent dehydration and possibly associated increased renal toxicity.

KETESSE can increase plasma urea nitrogen and creatinine. KETESSE can be associated with adverse effects on the renal system which can lead to glomerular nephritis, interstitial nephritis, renal papillary necrosis, nephrotic syndrome and acute renal failure.
Elderly patients are more likely to be suffering from impaired renal function (see section 4.2).
KETESSE is contraindicated in patients with moderate to severe renal dysfunction (creatinine clearance ≤ 59 mL/min) (see section 4.3).

Liver safety

Caution should be exercised in patients with impairment of hepatic functions.
KETESSE can cause increases in some liver parameters, and also significant increases in SGOT and SGPT. In case of a relevant increase in such parameters, therapy must be discontinued.
Elderly patients are more likely to be suffering from impaired hepatic function (see section 4.2).
KETESSE is contraindicated in patients with severely impaired hepatic function (Child-Pugh score 10 – 15) (see section 4.3).

Cardiovascular and cerebrovascular safety

Appropriate monitoring and advice are required for patients with history of hypertension and/or mild to moderate heart failure. Special caution should be exercised in patients with a history of cardiac disease, in particular those with previous episodes of heart failure as there is an increased risk of triggering heart failure, since fluid retention and oedema have been reported in association with NSAIDs therapy.

Clinical trial and epidemiological data suggest that the use of some NSAIDs (particularly at high doses and in long-term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for dexketoprofen, as in KETESSE.

Consequently, patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should not use KETESSE (see section 4.3).

KETESSE can inhibit platelet aggregation and prolong bleeding time via inhibition of prostaglandin synthesis. Therefore, its use in patients who are receiving other therapy that interferes with haemostasis, such as warfarin or other coumarins or heparins, is not recommended (see section 4.5).

Elderly patients are more likely to be suffering from impaired cardiovascular function (see section 4.2).

Skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported. Patients appear to be at highest risk of 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. KETESSE should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Other information

Particular caution is required in patients with:

- dehydration
- directly after major surgery.

Severe acute hypersensitivity reactions (e.g. anaphylactic shock) have been observed. Treatment must be discontinued at the first signs of severe hypersensitivity reactions following intake of KETESSE. Depending on the symptoms, any medically required procedures must be initiated by specialist health care providers.

Patients with asthma combined with chronic rhinitis, chronic sinusitis, and/or nasal polyposis have a higher risk of allergy to acetylsalicylic acid and/or NSAIDs than the rest of the population. Administration of KETESSE can cause asthma attacks or bronchospasm, particularly in subjects allergic to acetylsalicylic acid or NSAIDs (see section 4.3).
Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid the use of KETESSE in case of varicella.

KETESSE should be used with caution in patients suffering from haematopoietic disorders, systemic lupus erythematosus or mixed connective tissue disease.
KETESSE can mask the symptoms of infectious diseases.

Paediatric population

The safe use in children and adolescents has not been established.

4.5 Interaction with other medicines and other forms of interaction

The following interactions apply to nonsteroidal anti-inflammatory drugs (NSAIDs) in general:

Inadvisable combinations

- Other NSAIDs (including cyclooxygenase-2 selective inhibitors) and high doses of salicylates (≥ 3 g/day): administration of several NSAIDs together may increase the risk of gastrointestinal ulcers and bleeding, via a synergistic effect (see section 4.4).
- Anticoagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4), due to the high plasma protein binding of dexketoprofen and the inhibition of platelet function and damage to the gastroduodenal mucosa. If the combination cannot be avoided, close clinical observation and monitoring of laboratory values should be carried out.
- Heparins: increased risk of haemorrhage (due to the inhibition of platelet function and damage to the gastroduodenal mucosa). If the combination cannot be avoided, close clinical observation and monitoring of laboratory values should be carried out.
- Corticosteroids: there is an increased risk of gastrointestinal ulceration or bleeding (see section 4.4).
- Lithium: NSAIDs increase blood lithium levels, which may reach toxic values (decreased renal excretion of lithium). This parameter therefore requires monitoring during the initiation, adjustment and withdrawal of treatment with KETESSE.
- Methotrexate, used at high doses of 15 mg/week or more: increased haematological toxicity of methotrexate via a decrease in its renal clearance by anti-inflammatory medicines in general.
- Hydantoines and sulfonamides: the toxic effects of these substances may be increased.

Combinations requiring precautions

- Diuretics, angiotensin-converting-enzyme (ACE) inhibitors, antibacterial aminoglycosides and angiotensin II receptor antagonists: dexketoprofen may reduce the effect of diuretics and antihypertensive medicines. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of medicines that inhibit cyclo-oxygenase and ACE inhibitors, angiotensin II receptor antagonists or antibacterial aminoglycosides may result in further deterioration of renal function, which is usually reversible. In case of combined prescription of dexketoprofen, as in

KETESSE, and a diuretic, it is essential to ensure that the patient is adequately hydrated and to monitor renal function at the start of the treatment (see section 4.4).

- Methotrexate, used at low doses, less than 15 mg/week: increased haematological toxicity of methotrexate via a decrease in its renal clearance by anti-inflammatory medicines in general. Weekly monitoring of blood count during the first weeks of the combination. Increased surveillance in the presence of even mildly impaired renal function, as well as in the elderly.
- Pentoxifylline: increased risk of bleeding. Increase clinical monitoring and check bleeding time more often.
- Zidovudine: risk of increased red cell line toxicity via action on reticulocytes, with severe anaemia occurring one week after the NSAID is started. Check complete blood count and reticulocyte count one to two weeks after starting treatment with the NSAID.
- Sulfonylureas: NSAIDs can increase the hypoglycaemic effect of sulfonylureas by displacement from plasma protein binding sites.

Combinations needing to be taken into account

- Beta-blockers: treatment with an NSAID may decrease their antihypertensive effect via inhibition of prostaglandin synthesis.
- Ciclosporin and tacrolimus: nephrotoxicity may be enhanced by NSAIDs via renal prostaglandin mediated effects. During combination therapy, renal function has to be measured.
- Thrombolytics: increased risk of bleeding.
- Antiplatelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).
- Probenecid: plasma concentrations of dexketoprofen may be increased; this interaction can be due to an inhibitory mechanism at the site of renal tubular secretion and of glucuronoconjugation, and requires adjustment of the dose of KETESSE.
- Cardiac glycosides: NSAIDs may increase plasma glycoside concentration.
- Mifepristone: there is a theoretical risk that prostaglandin synthetase inhibitors may alter the efficacy of mifepristone. Limited evidence suggests that co-administration of NSAIDs on the

day of prostaglandin administration does not adversely influence the effects of mifepristone or the prostaglandin on cervical ripening or uterine contractility and does not reduce the clinical efficacy of medical termination of pregnancy.

- Quinolone antibiotics: animal data indicate that high doses of quinolones in combination with NSAIDs can increase the risk of developing convulsions.
- Tenofovir: concomitant use with NSAIDs can increase plasma urea nitrogen and creatinine, renal function should be monitored in order to control a potential synergic influence on renal function.
- Deferasirox: concomitant use with NSAIDs can increase the risk of gastrointestinal toxicity. Close clinical monitoring is required when deferasirox is combined with these substances.
- Pemetrexed: concomitant use with NSAIDs may decrease pemetrexed elimination, therefore caution should be taken when administering higher doses of NSAIDs. In patients with mild to moderate renal insufficiency (creatinine clearance from 45 to 79 mL/min), the concomitant administration of pemetrexed with NSAIDs doses should be avoided for 2 days before and 2 days following pemetrexed administration.

4.6 Fertility, pregnancy and lactation

KETESSE is contraindicated during third trimester of pregnancy and lactation (see section 4.3).

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/-fetal development. Data from epidemiological studies raise concern about an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a 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- fetal lethality. In addition, increased incidences of various malformations including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During

pregnancy, KETESSE should not be given.

During the third trimester of pregnancy, KETESSE may expose the fetus to:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydramnios;

At the end of pregnancy, KETESSE may expose the mother and the neonate 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.

Breastfeeding

It is not known whether dexketoprofen is excreted in human milk. KETESSE is contraindicated during breastfeeding (see section 4.3).

Fertility

The use of KETESSE may impair female fertility and is not recommended in women attempting to conceive.

4.7 Effects on ability to drive and use machines

KETESSE may cause undesirable effects such as dizziness, visual disturbances or drowsiness (see section 4.8). The ability to react and the ability to take part actively in road traffic and to operate machines may be impaired in these cases.

4.8 Undesirable effects

The adverse events reported in clinical trials are tabulated below, classified by system organ class and ordered by frequency:

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 (< 1/10 000)**
Blood and lymphatic system disorders	---	---	---	Neutropenia, thrombocytopenia
Immune system disorders	---	---	Laryngeal oedema	Anaphylactic reaction, including anaphylactic shock
Metabolism and nutrition disorders	---	---	Anorexia	---
Psychiatric disorders	---	Insomnia, anxiety	---	---
Nervous system disorders	---	Headache, dizziness, somnolence	Paraesthesia, syncope	---
Eye disorders	---	---	---	Blurred vision
Ear and labyrinth disorders	---	Vertigo	---	Tinnitus
Cardiac disorders	---	Palpitations	---	Tachycardia
Vascular disorders	---	Flushing	Hypertension	Hypotension
Respiratory, thoracic and mediastinal	---	---	Bradypnoea	Bronchospasm, dyspnoea

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 (< 1/10 000)**
disorders				
Gastrointestinal disorders	Nausea and/or vomiting, abdominal pain, diarrhoea, dyspepsia	Gastritis, constipation, dry mouth, flatulence	Peptic ulcer, peptic ulcer haemorrhage or peptic ulcer perforation (see section 4.4)	Pancreatitis
Hepatobiliary disorders	---	---	Hepatocellular injury	
Skin and subcutaneous tissue disorders	---	Rash	Urticaria, acne, sweating increased	Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), angioedema, facial oedema, photosensitivity reaction, pruritus
Musculoskeletal and connective tissue disorders	---	---	Back pain	---
Renal and urinary disorders	---	---	Acute renal failure, polyuria	Nephritis or nephrotic syndrome

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 (< 1/10 000)**
Reproductive system and breast disorders	---	---	Menstrual disorder, prostatic disorder	---
General disorders and administration site conditions	---	Fatigue, pain, asthenia, rigors, malaise	Peripheral oedema	---
Investigations	---	---	Liver function test abnormal	---

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal 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 4.3) have been reported following administration. Less frequently, gastritis has been observed. Oedema, hypertension and cardiac failure have been reported in association with NSAIDs treatment.

The following undesirable effects may appear: aseptic meningitis, which might predominantly occur in patients with systemic lupus erythematosus or mixed connective tissue disease; haematological reactions (purpura, aplastic and haemolytic anaemia, and rarely agranulocytosis and medullar hypoplasia).

Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare).

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long-term treatment) may be associated with a small increased risk of arterial thrombotic

events (for example myocardial infarction or stroke) (see section 4.4).

Post-marketing experience

SYSTEM ORGAN CLASS	**Not known** **(Can not be estimated from the available data)**
Metabolism and nutrition disorders	Hypokalaemia*
Renal and urinary disorders	Renal tubular acidosis*

*See sections 4.4 and 4.9. Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of NSAIDs at higher than recommended doses.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of KETESSE is important. It allows continued monitoring of the benefit/risk balance of KETESSE. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

The symptomatology following overdose is not known. Similar medicines have produced gastrointestinal (vomiting, anorexia, abdominal pain) and neurological (somnolence, vertigo, disorientation, headache) disorders.

In case of accidental or excessive intake, immediately institute symptomatic therapy according to the patient's clinical condition. Activated charcoal should be administered if more than 5 mg/kg has been ingested by an adult or a child within an hour.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see sections 4.4 and section 4.8).

Dexketoprofen trometamol may be removed by dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

Pharmacotherapeutic group: Propionic acid derivatives.

ATC code: M01AE17.

Dexketoprofen trometamol is the tromethamine salt of *S*-(+)-2-(3-benzoylphenyl) propionic acid, an analgesic, anti-inflammatory and antipyretic medicine, which belongs to the nonsteroidal anti-inflammatory group of medicines (M01AE).

Pharmacodynamic effects

Dexketoprofen has been demonstrated to be an inhibitor for COX-1 and COX-2 activities in experimental animals and humans.

Clinical efficacy and safety

Clinical studies performed on several pain models demonstrated effective analgesic activity of dexketoprofen. The onset of the analgesic activity was obtained in some studies at 30 minutes post-administration. The analgesic effect persists for 4 to 6 hours.

5.2 Pharmacokinetic properties

Absorption

After oral administration of dexketoprofen trometamol to humans, the C_{max} is reached at 30 min (range 15 to 60 min).

When administered concomitantly with food, the AUC does not change, however the C_{max} of dexketoprofen decreases and its absorption rate is delayed (increased t_{max}).

Distribution

The distribution half-life and elimination half-life values of dexketoprofen are 0,35 and 1,65 hours,

respectively. As with other medicines with a high plasma protein binding (99 %), its volume of distribution has a mean value below 0,25 L/kg.

In multiple-dose pharmacokinetic studies, it was observed that the AUC after the last administration is not different from that obtained following a single dose, indicating that no medicine accumulation occurs.

Biotransformation

After administration of dexketoprofen trometamol only the *S*-(+) enantiomer is obtained in urine, demonstrating that no conversion to the *R*-(-) enantiomer occurs in humans.

Elimination

The main elimination route for dexketoprofen is glucuronide conjugation followed by renal excretion.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch

Microcrystalline cellulose

Sodium starch glycollate

Glycerol distearate

Hypromellose

Titanium dioxide

Propylene glycol

Macrogol 6000.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

Store at or below 25 °C.

6.4 Special precautions for storage

Keep the blister strips in the outer carton until required for use.

Do not remove the tablets from the blister strips until required for use.

6.5 Nature and contents of container

Opaque white or transparent PVC/aluminium or aluminium/aluminium blister strips in an outer carton.

Pack sizes: 4, 10, 20, 30, 50 or 500 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Menarini South Africa (Pty) Ltd

Waterside Place, Unit 02D, South Gate Office Park

Carl Cronje Drive, Tygervalley

Cape Town 7530

Tel: + 27 21 109 6444

8. REGISTRATION NUMBER

KETESSE 25 mg: 54/2.7/0536

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

27 July 2021

10. DATE OF REVISION OF THE TEXT

To be allocated by the Authority.