SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Diclomax SR.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Diclomax SR capsule contains diclofenac sodium 75mg.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Modified release capsules for oral use.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For rheumatoid arthritis; osteoarthritis; low back pain; acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations; relief of pain in fractures; ankylosing spondylitis; acute gout; control of pain and inflammation in orthopaedic, dental and other minor surgery.

4.2 Posology and method of administration

For oral use.

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

Adults

One or two 75mg capsules daily taken whole in single or divided doses preferably with food or after food.

Children

Not recommended.

Elderly

The elderly are at an increased risk of serious consequences of adverse reactions. Studies indicate the pharmacokinetics of diclofenac sodium are not impaired to any clinical extent in the elderly, however, as with all non-steroidal anti-inflammatory drugs, Diclomax should be used with caution in elderly patients and the lowest effective dose used for the shortest possible duration. These patients should be monitored regularly for GI bleeding during NSAID therapy.

4.3 Contraindications

- Known hypersensitivity to diclofenac sodium or to any of the excipients.
- Active gastric or intestinal ulcer, bleeding or perforation.
- History of gastrointestinal (GI) bleeding or perforation, related to previous non-steroidal anti-inflammatory drug (NSAID) therapy.
- Active or history of recurrent peptic ulcer or haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other NSAIDs.
- Acute porphyria.
- Severe hepatic, renal or cardiac failure (see section 4.4).
- During the last trimester of pregnancy (see section 4.6).
- Established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

4.4 Special warnings and precautions for use

General:

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).

Caution is indicated in the elderly on basic medical grounds. As with all NSAIDs, Diclomax should only be given to the elderly after other forms of treatment have been carefully considered, as the elderly have an increased frequency of adverse reactions to NSAIDs especially GI bleeding and perforation which may be fatal (see section 4.2). In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight.

The use of Diclomax with concomitant systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects (see section 4.5).

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur in rare cases with diclofenac without earlier exposure

to the drug. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction. Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to diclofenac.

Like other NSAIDs, diclofenac may mask the signs and symptoms of infection due to its pharmacodynamic properties.

As Diclomax contains lactose, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

As Diclomax contains sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Diclomax contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

Gastrointestinal effects:
GI bleeding, ulceration or perforation, which can be fatal, has been reported with NSAID therapy, including diclofenac, and can occur at any time during treatment, with or without warning symptoms or a previous history of serious GI events. They generally have more serious consequences in the elderly. If GI bleeding or ulceration occurs in patients receiving Diclomax, the treatment should be withdrawn.

As with all NSAIDs, including diclofenac, close medical surveillance is imperative and particular caution should be exercised when prescribing diclofenac in patients with symptoms indicative of GI disorders or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation (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.

To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly, the treatment should be initiated and maintained at the lowest effective dose.

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 GI risk (see below and section 4.5).

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

Caution is advised in patients receiving concomitant medications that could increase the risk of ulceration or bleeding, such as systemic corticosteroids,

anticoagulants such as warfarin, anti-platelet agents such as aspirin or selective serotonin-reuptake inhibitors (see section 4.5).

Close medical surveillance and caution should also be exercised in patients with ulcerative colitis or Crohn's disease, as their condition may be exacerbated (see section 4.8).

NSAIDs, including diclofenac, may be associated with increased risk of GI anastomotic leak. Close medical surveillance and caution are recommended when using diclofenac after GI surgery.

Hepatic effects:
Close medical surveillance is required when prescribing Diclomax to patients with impaired hepatic function, as their condition may be exacerbated.

As with other NSAIDs, including diclofenac, values of one or more liver enzymes may increase. During prolonged treatment with Diclomax, regular monitoring of hepatic function is indicated as a precautionary measure. If abnormal liver function tests persist or worsen, if clinical signs or symptoms consistent with liver disease develop, or if other manifestations occur (e.g. eosinophilia, rash), Diclomax should be discontinued. Hepatitis may occur with use of diclofenac without prodromal symptoms.

Caution is called for when using Diclomax in patients with hepatic porphyria, since it may trigger an attack (see section 4.3).

Renal effects:
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.

As fluid retention and oedema have been reported in association with NSAID therapy, including diclofenac, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and in those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery (see section 4.3). Monitoring of renal function is recommended as a precautionary measure when using Diclomax in such cases. Discontinuation of therapy is usually followed by recovery to the pre-treatment state.

Cardiovascular and cerebrovascular effects:

Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration. As the cardiovascular risks of diclofenac 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.

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure (see section 4.3) as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data consistently point towards an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150mg daily) and in long term treatment (see section 4.3).

Respiratory disorders:
In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions on NSAIDs like asthma exacerbations (so-called intolerance to analgesics / analgesics-asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients (readiness for emergency). This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

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

Haematological:
During prolonged treatment with diclofenac, as with other NSAIDs, monitoring of the blood count is recommended.

Diclomax, in common with other NSAIDs, can reversibly inhibit platelet aggregation. Patients with defects of haemostasis should be carefully monitored.

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).

Skin reactions:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and generalised bullous fixed drug eruption have been reported very rarely in association with the use of diclofenac (see section 4.8). 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. Diclomax should be

discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Impaired Female fertility:
The use of Diclomax 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 Diclomax should be considered.

4.5 Interactions with other medicinal products and other forms of interaction

Lithium: Diclofenac may increase plasma concentrations and decrease elimination of lithium. Monitoring of the serum lithium level is recommended.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure and reduce GFR. If used concomitantly, diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.

Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding (see section 4.4). Although clinical investigations do not appear to indicate that diclofenac affects the action of anticoagulants, there are reports of an increased risk of haemorrhage in patients receiving diclofenac and anticoagulants concomitantly. Close monitoring of such patients is therefore recommended.

Antidiabetic agents: Clinical studies have shown that Diclomax can be given together with oral hypoglycaemic agents without influencing their clinical effect. However, there have been isolated reports of hyperglycaemic and hypoglycaemic effects, which have required adjustments to the dosage of hypoglycaemic agents. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

Ciclosporin: Ciclosporin nephrotoxicity may be increased by the effect of NSAIDs, including diclofenac, on renal prostaglandins. Therefore, Diclomax should be given at doses lower than those that would be used in patients not receiving ciclosporin.

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

Methotrexate: Diclofenac can inhibit the tubular renal clearance of methotrexate thereby increasing methotrexate levels. Caution should be exercised if NSAIDs, including diclofenac, and methotrexate are administered within 24 hours of each other, since NSAIDs may increase methotrexate plasma levels with decreased elimination, resulting in increased toxicity.

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. There

have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs.

Selective serotonin reuptake inhibitors (SSRIs): Increased risk of GI bleeding (see section 4.4).

Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more systemic NSAIDs (including aspirin) as this may increase the risk of adverse events (see section 4.4).

Corticosteroids: Systemic corticosteroids can increase the risk of GI ulceration or bleeding (see section 4.4).

Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity. Concomitant treatment with potassium-sparing drugs may be associated with increased serum potassium levels, which should therefore be monitored frequently (see section 4.4).

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

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.

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Colestipol and colestyramine: These agents can induce a delay or decrease in absorption of diclofenac. Therefore, it is recommended to administer diclofenac at least one hour before or 4 to 6 hours after administration of colestipol or colestyramine.

Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentration and exposure to diclofenac due to inhibition of diclofenac metabolism.

4.6 **Fertility, pregnancy and lactation**

Pregnancy:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest 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-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, diclofenac 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, diclofenac should not be given unless clearly necessary. If diclofenac 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 diclofenac for several days from gestational week 20 onward. Diclofenac 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, which may progress to renal failure with oligohydramnios (see above);

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, diclofenac is contraindicated during the third trimester of pregnancy.

Lactation:
In limited studies so far available, diclofenac can appear in breast milk in very low concentrations with traces of diclofenac sodium found in breast milk following oral doses of 50mg every eight hours. Therefore, diclofenac should not be administered during breastfeeding in order to avoid undesirable effects in the infant.

Fertility:
The use of diclofenac 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 diclofenac should be considered.

4.7 Effects on ability to drive and use machines

Patients who experience visual disturbances, dizziness, vertigo, somnolence, central nervous system disturbances, drowsiness or fatigue while taking NSAIDs should refrain from driving or operating machinery.

4.8 Undesirable effects

Adverse reactions are ranked under the heading of frequency, the most frequent first, using the following convention: very common: (>1/10); common (≥ 1/100, <1/10); uncommon (≥ 1/1,000, <1/100); rare (≥1/10,000, <1/1000); very rare (<1/10,000); not known: cannot be estimated from the available data.

The following undesirable effects include those reported with either short-term or long-term use.

Blood and lymphatic system disorders	
Very rare	Thrombocytopenia, leucopenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.
Not known	Neutropenia.
Immune system disorders	
Rare	Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock).
Very rare	Angioneurotic oedema (including face oedema).
Psychiatric disorders	
Very rare	Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Not known	Confusion, hallucinations.
Nervous system disorders	
Common	Headache, dizziness.
Rare	Somnolence.
Very rare	Paraesthesia, memory impairment, convulsion, anxiety, tremor, 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; taste disturbances, cerebrovascular accident.
Not known	Optic neuritis.
Eye disorders	
Very rare	Visual disturbance, vision blurred, diplopia.
Ear and labyrinth disorders	
Common	Vertigo.

Very rare	Tinnitus, hearing impaired.
Cardiac disorders	
Very rare	Palpitations, chest pain, cardiac failure, myocardial infarction.
Not known	Kounis syndrome
Vascular disorders	
Very rare	Hypertension, vasculitis.
Respiratory, thoracic and mediastinal disorders	
Rare	Asthma (including dyspnoea).
Very rare	Pneumonitis.
Not known	Aggravated asthma, bronchospasm.
Gastrointestinal disorders	
Common	Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia.
Rare	Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer (with or without bleeding or perforation) sometimes fatal particularly in the elderly.
Very rare	Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.
Not known	Ischaemic colitis
Hepatobiliary disorders	
Common	Transaminases increased.
Rare	Hepatitis, jaundice, liver disorder.
Very rare	Fulminant hepatitis, hepatic necrosis, hepatic failure.
Skin and subcutaneous tissue disorders	
Common	Rash.
Rare	Urticaria.
Very rare	Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.
Not known	Fixed drug eruption, generalised bullous fixed drug eruption.
Renal and urinary disorders	
Very rare	Acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis.
General disorders and administration site conditions	
Rare	Oedema.
Not known	Fatigue, malaise.

Clinical trial and epidemiological data consistently point towards an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150mg daily) and in long term treatment (see sections 4.3 and 4.4).

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

4.9 Overdose

(a) Symptoms

There is no typical clinical picture resulting from diclofenac over dosage. Symptoms can include headache, nausea, vomiting, epigastric pain, GI bleeding, diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, or convulsions. In cases of significant poisoning, acute renal failure and liver damage are possible.

(b) Therapeutic Measures

Management of acute poisoning with NSAIDs, including diclofenac, essentially consists of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, GI disorder, and respiratory depression.

Special measures such as forced diuresis, dialysis or haemo-perfusion are probably of no help in eliminating NSAIDs, including diclofenac, due to the high protein binding and extensive metabolism.

Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life-threatening overdose.

Renal and liver function should be closely monitored.

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

Frequent or prolonged convulsions should be treated with intravenous diazepam.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Acetic acid derivatives and related substances, ATC Code: M01A B05

Diclofenac Sodium is a non-steroidal agent with marked analgesic/anti-inflammatory and anti-pyretic properties. It is an inhibitor of prostaglandin synthetase (cyclo-oxygenase).

5.2 Pharmacokinetic properties

Diclofenac Sodium is rapidly absorbed from the gut and is subject to first-pass metabolism. Diclomax Capsules give peak plasma concentrations after approximately 2.5 hours. The active substance is 99.7% protein bound and plasma half-life for the terminal elimination phase is 1-2 hours. Approximately 60% of the administered dose is excreted via the kidneys in the form of metabolites and less than 1% in unchanged form. About 30% of the dose is excreted via the bile in metabolised form.

The Diclomax slow release preparation:

- Increases the duration of action of the drug
- Maintains relatively constant rate of absorption in the gastro-intestinal tract over a longer period of time
- Increases the fraction of the ingested dose absorbed in the GI tract
- Regulates the rate at which the drug is made available for absorption, thereby reducing the possibility of malabsorption and occurrence of side-effects.

5.3 Preclinical safety data

The results of the preclinical tests do not add anything of further significance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Maize starch

Polyethylene glycol 6000

Ammonio methacrylate copolymer type A

Talc

Lactose

Polysorbate 80

Purified water

Ethanol 96%

Acetone

Capsule Shell Constituents:

Gelatin

Yellow iron oxide (E172)

Titanium dioxide (E171)

Overprint Ink Constituents:

Shellac glaze

Propylene glycol

Black iron oxide (E172)

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months – PVC/PE/PVDC blister packs.
18 months – PVC blister packs.
60 months – Polyamide/Al/PVC-Al blister packs.

6.4 Special precautions for storage

PVC/PE/PVDC and PVC blister packs: Store between 10^{o}C and 25^{o}C. Protect from moisture. Do not refrigerate.

Polyamide/Al/PVC-Al blister packs: This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

White opaque PVC blister pack with hard tempered foil or white opaque PVC/PE/PVDC/hard tempered foil blister strips or Polyamide/Al/PVC-Al blister strips.

Packs of 4 and 56 capsules.

6.6 Special precautions for disposal

No special instructions needed.

7 MARKETING AUTHORISATION HOLDER

Galen Limited
Seagoe Industrial Estate
Craigavon
BT63 5UA
UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 27827/0004.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12 January 1995.

10 DATE OF REVISION OF THE TEXT

13/08/2025