Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Otriflu 12.5mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 12.5 mg diclofenac potassium.

Excipient with known effect: Lactose monohydrate (33.450mg)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet (Tablets).
White oblong (capsule-shaped) film coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Relief of painful conditions such as headache, dental pain, period pain, rheumatic and muscular pain, backache. Relief of symptoms of colds and flu, including fever.

4.2 Posology and method of administration

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

Adults and children aged 14 years and over:
For oral administration:
Initially two tablets, followed by one or two tablets every 4 to 6 hours as needed. No more than 6 tablets (75 mg) should be taken in any 24 hour period. Otriflu is intended for short-term use, up to 5 days for relief of pain and 3 days for relief of fever.
The tablets should be swallowed whole with a drink of water, preferably with or after food.

Special population
Children and adolescents below 14 years:
Otriflu tablets are not recommended for use in children under 14 years of age.

Renal impairment
Otriflu is contraindicated in patients with renal failure (see section 4.3 Contraindications).
No specific studies have been carried out in patients with renal impairment; therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Otriflu to patients with mild to moderate renal impairment (See section 4.4. Special warnings and precautions for use).

Hepatic impairment
Otriflu is contraindicated in patients with severe hepatic impairment (see section 4.3 Contraindications).
No specific studies have been carried out in patients with hepatic impairment; therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Otriflu to patients with mild to moderate hepatic impairment (See section 4.4. Special warnings and precautions for use).

Elderly:
Although the pharmacokinetics of diclofenac are not impaired to any clinically relevant extent in elderly patients, non-steroidal anti-inflammatory drugs should be used with particular caution in older patients who generally are more prone to adverse reactions. The patient should be monitored regularly for GI bleeding during NSAID therapy.

4.3 Contraindications

- Known hypersensitivity to the active substance or to any of the excipients (listed in section 6.1).
- Active gastric or intestinal ulcer, bleeding or perforation.
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Like other non-steroidal anti-inflammatory drugs (NSAIDs), Diclofenac is also contraindicated in patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or other NSAIDs.
- Severe hepatic or renal failure (see section 4.4 Special warnings and precautions).
- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease.
- Last trimester of pregnancy (see section 4.6 Pregnancy and lactation).

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 4.2, and GI and cardiovascular risks below). The concomitant use of Otriflu with systemic NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided due to the potential for additive undesirable effects. Caution is indicated in the elderly on basic medical grounds. In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight.

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2). As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur in rare cases with diclofenac without earlier exposure to the drug. Like other NSAIDs, Diclofenac may mask the signs and symptoms of infection due to its pharmacodynamic properties.

Otriflu 12.5 mg contains lactose and therefore are not recommended for patients with rare hereditary problems of galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Gastrointestinal effects:
GI bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs may 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 gastrointestinal bleeding or ulceration occurs in patients receiving Diclofenac, the medicinal product 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 gastrointestinal (GI) disorders or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation (see 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). GI bleeding, ulceration or perforation may occur at any time during treatment. The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

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 gastrointestinal risk (see below and 4.5).
Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding).
Caution is recommended 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 anti-platelet agents such as aspirin (see section 4.5). When GI bleeding or ulceration occurs in patients receiving diclofenac, the treatment should be withdrawn.

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 4.8).

Hepatobiliary effects:
Close medical surveillance is required when prescribing Diclofenac 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 Diclofenac, 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), Diclofenac should be discontinued. Hepatitis may occur with use of diclofenac without prodromal symptoms. Caution is called for when using Diclofenac in patients with hepatic porphyria, since it may trigger an attack.

Renal effects:
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 4.3). Monitoring of renal function is recommended as a precautionary measure when using Diclofenac in such cases. Discontinuation of therapy is usually followed by recovery to the pre-treatment state.

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

Cardiovascular and cerebrovascular effects:
Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes, mellitus and smoking) should only be treated with diclofenac after careful conditions.

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. Patients should be advised to seek further medical advice if symptoms persist or do not improve within the recommended durations of treatment.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with diclofenac after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus and smoking).

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 (150 mg daily) and in long-term treatment.

Patients should remain alert for the signs and symptoms of serious thrombotic events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warning symptoms. Patients should be instructed to see a physician immediately in case of such an event.

Haematologic effects:
During prolonged treatment with Diclofenac, as with other NSAIDs, monitoring of the blood count is recommended. Like other NSAIDs, Diclofenac may temporarily inhibit platelet aggregation. Patients with defects of haemostasis should be carefully monitored.

Respiratory effects (pre-existing asthma):
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.

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).

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 (see section 4.4).

Antihypertensives: Reduced antihypertensive effect.

Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, which should therefore be monitored.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce glomerular filtration rate and increase plasma glycoside levels.

Lithium: Decreased elimination of lithium.

Methotrexate: Decreased elimination of methotrexate. Caution is called for if NSAIDs are administered less than 24 hours before or after treatment with methotrexate, as the toxicity of this substance may be increased.

Ciclosporin: Increased risk of nephrotoxicity.

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

Anticoagulants <u>and anti-platelet agents</u>: 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.

Quinolone antibacterials: 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).

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.

Antidiabetics: 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 which have required adjustment to the dosage of hypoglycaemic agents.

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. 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.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, 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, diclofenac is contraindicated during the third trimester of pregnancy.

Lactation:
Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, Diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant.

Fertility
As with other NSAIDs, the use of diclofenac potassium 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 potassium should be considered.

4.7 Effects on ability to drive and use machines

Patients experiencing visual disturbances, dizziness, vertigo, somnolence or other central nervous system disturbances while taking Diclofenac, should refrain from driving or using machines.

4.8 Undesirable effects

Undesirable effects include those associated with short-term or long-term use of other pharmaceutical forms of diclofenac as well as those reported with Otriflu tablets.

Gastrointestinal safety of NSAIDS
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 Special warnings and precautions for use). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4 Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.

Cardiovascular safety of NSAIDS
Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

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

The following adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), including isolated reports.

Blood and lymphatic system disorders
Very rare: Thrombocytopenia, leucopenia, anaemia (including haemolytic anaemia, and aplastic anaemia), agranulocytosis.

Immune system disorders
Rare: Hypersensitivity reactions such as asthma, systemic, 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 reactions.

Nervous system disorders
Common: Headache, dizziness, vertigo
Rare: Somnolence, drowsiness.
Very rare: Paraesthesias, memory impairment, convulsions, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident.

Eye disorders
Very rare: Visual disturbances (blurred vision, diplopia)

Ear and labyrinth disorders
Common: Vertigo.
Very rare: Tinnitus, hearing impaired.

Cardiac disorders:
Very rare: Palpitations, chest pain, hypertension, cardiac failure, myocardial infarction.

Vascular disorders
Rare: hypotension.
Very rare: hypertension, vasculitis.

Respiratory, thoracic and mediastinal disorders:
Rare: Asthma (including dyspnoea).
Very rare: Pneumonitis.

Gastrointestinal tract disorders
Common: Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia.

Rare: Gastritis, gastrointestinal haemorrhage, (haematemesis, melaena, diarrhea, haemorrhagic melaena) gastric or intestinal ulcer (with or without bleeding or perforation).
Very rare: Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis, glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.
Frequency not known: Ischaemic colitis.

Hepatobiliary disorders
Common: Transaminases increased.
Rare: Hepatitis, with or without jaundice, liver disorder.
Very rare: Fulminant hepatitis.

Skin and subcutaneous tissue disorders
Common: Rashes.
Rare: Urticaria.
Very rare: Bullous eruptions, eczema, erythema, multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.

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.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that the use of diclofenac, particularly at high doses (150 mg daily) 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 Special warnings and precautions for use).

4.9 Overdose

Symptoms:
There is no typical clinical picture resulting from diclofenac over dosage. Over dosage can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

Therapeutic measures:
Management of acute poisoning with NSAIDs consists essentially of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal 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.

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.
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
ATC codes M01AB (antiinflammatory/antirheumatic products, non-steroids) & N02B (analgesics and antipyretics).

Mechanism of action and pharmacodynamic effects
Otriflu tablets contain diclofenac potassium, a non-steroidal compound with pronounced analgesic, anti-inflammatory and antipyretic properties.
Otriflu tablets have a rapid onset of action making them particularly suitable for the treatment of acute painful conditions, and for the reduction of fever. Inhibition of prostaglandin biosynthesis is considered to be fundamental to the mechanism of action. Prostaglandins play a major role in causing inflammation, pain and fever.
Diclofenac potassium *in vitro* does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in humans.

5.2 Pharmacokinetic properties

Absorption
Diclofenac is rapidly and completely absorbed. Mean peak plasma concentrations of 2.15μmol/L are attained after approximately 30 minutes (median Tmax) following ingestion of two 12.5 mg tablets.
Since about half of diclofenac is metabolised during its first passage through the liver (“first pass” effect), the area under the concentration curve is about half as large following oral administration as it is following a parenteral dose of equal size.
Pharmacokinetic behaviour does not change after repeated administration. No accumulation occurs provided the recommended dosage intervals are observed.

Distribution
99.7% of diclofenac binds to serum proteins, mainly to albumin (99.4%). The apparent volume of distribution is 0.12-0.17 L/kg. Diclofenac enters the synovial fluid, where maximum concentrations are measured 2-4 hours after peak plasma values have been reached. The apparent half-life for elimination from the synovial fluid is 3-6 hours. Two hours after reaching peak plasma levels, concentrations of the active substance are already higher in the synovial fluid than in the plasma, and they remain higher for up to 12 hours.

Biotransformation
Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates.

Two of these phenolic metabolites are biologically active, but to a much lesser extent than diclofenac.

Elimination
Total systemic clearance of diclofenac from plasma is 263 ± 56 ml/min. The terminal half-life in plasma is 1 to 2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. A fifth metabolite, 3’-hydroxy-4’-methoxy-diclofenac, has a much longer plasma half-life. This metabolite is virtually inactive.
About 60% of the administered dose is excreted in the urine as the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites through the bile in the faeces.

Linearity/non-linearity
The extent of absorption (AUC) is in linear proportion to the size of the dose.

Characteristics in patients
No relevant age-dependent differences in the drug’s absorption, metabolism, or excretion have been observed.

In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single dose kinetics when applying the usual dosage schedule. At a creatinine clearance of less than 10 ml/min, the calculated steady-state plasma levels of the hydroxy metabolites are about 4 times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.

In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 Preclinical safety data

Diclofenac did not influence fertility of the parent animals (rats) nor the pre-, peri- and postnatal development of the offspring. No teratogenic effects were detected in mice, rats and rabbits. No mutagenic effects could be demonstrated in various *in vitro* and *in vivo* experiments, and no carcinogenic potential was detected in long-term studies in rats and mice.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Collodal Anhydrous Silica
Lactose Monohydrate
Maize starch
Sodium starch glycolate
Povidone
Microcrystalline cellulose
Magnesium stearate

Coating:
Hypromellulose
Titanium dioxide
Microcrystalline cellulose
Stearic acid

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Opaque of transparent PVC/Polychlorotrifluoroethylene/PVC/Aluminium blister pack
Pack size: 10, 20 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The tablets should be swallowed whole with liquid, preferably before meals.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/137/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd December 2009

Date of last renewal: 21st December 2014

10 DATE OF REVISION OF THE TEXT

July 2017