SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE PRODUCT

EFRIDOL 100 mg tablets
EFRIDOL 100 mg granules for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg of nimesulide.
Each sachet of granules for oral suspension contains 100 mg of nimesulide.

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Tablets, granules for oral suspension

4. CLINICAL INFORMATION

4.1 Therapeutic indications

Treatment of acute pain (see section 4.2).

Primary dysmenorrhoea.

Nimesulide should be prescribed only as second-line treatment. The decision to prescribe nimesulide should be based on an assessment of the individual patient's overall risks (see sections 4.3 and 4.4).

4.2 Posology and method of administration

EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) should be used for the shortest possible time, according to clinical needs. Furthermore, side effects can be minimized by using the lowest effective dose for the shortest time necessary to control symptoms (see section 4.4).
The maximum duration of a treatment cycle with nimesulide is 15 days.

Adults:
100 mg twice daily after meals.

Elderly:
It is not necessary to reduce the daily dose for elderly patients (see section 5.2).

Children (<12 years):
EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is contraindicated for these patients (see also section 4.3).

Adolescents (12 to 18 years):
Based on the kinetic profile in adults and the pharmacodynamic characteristics of nimesulide, no dosage adjustment is necessary in these patients.

Renal insufficiency:
Based on the pharmacokinetics there is no need to adjust the dose in patients with mild to moderate renal insufficiency (creatinine clearance 30-80 ml/min); EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) are contraindicated in the case of renal impairment (creatinine clearance <30 ml/min) (see sections 4.3 and 5.2).

Liver failure:
The use of 100 mg tablets EFRIDOL (or 100 mg granules for oral suspension) are contraindicated in patients with liver failure (see sections 4.3 and 5.2).

4.3 Contraindications

Hypersensitivity to nimesulide or any of the excipients.

History of hypersensitivity reactions (e.g., bronchospasm, rhinitis, urticaria, nasal polyps) in response to acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs.
Previous hepatotoxic reactions to nimesulide.
Concomitant exposure to other potentially hepatotoxic substances.
Alcoholism, drug addiction.
History of gastrointestinal bleeding or perforation related to prior treatment with NSAIDs.
Recurrent active Haemorrhage/peptic ulcer or patient has had this in the past (two or more distinct episodes of proven ulceration or bleeding).
Cerebrovascular bleeding or other bleeding or bleeding disorders in progress.
Severe coagulation disorders.
Severe heart failure.
Severe renal impairment.
Liver failure.
Patients with fever and/or flu symptoms.
Children under 12 years of age.
Third trimester of pregnancy and lactation (see sections 4.6 and 5.3).

4.4 Special warnings and precautions for use

The use of EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) should be avoided concurrently with NSAIDs, including selective inhibitors of cyclooxygenase-2. In addition, patients should be advised to refrain from taking other analgesics concomitantly.

Side effects can be minimized by using the lowest effective dose for the shortest time necessary to control symptoms (see section 4.2).

Suspend treatment if benefits are not observed.

Effects on the liver

In rare cases an association between EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) and serious liver reactions has been reported, including some very rare fatal cases (see also section 4.8). Patients who experience symptoms consistent with liver damage during treatment with EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) (e.g., anorexia, nausea, vomiting, abdominal pain, fatigue, dark urine) or who have abnormal liver function tests during treatment should discontinue treatment. These patients should no longer use nimesulide. Liver damage, reversible in most cases, was reported after short exposure to the drug.

In the case in which patients taking nimesulide develop a fever and/or flu-like symptoms, treatment should be discontinued.

Gastrointestinal effects

Gastrointestinal bleeding, ulceration and perforation

During treatment with all NSAIDs, at any time with or without warning symptoms or previous history of gastrointestinal events, GI bleeding, ulceration and perforation which may be fatal have been reported.

The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing doses of NSAIDs in patients with a history of ulcers, particularly when complicated by haemorrhage or perforation (see section 4.3) and in the elderly. These patients should begin treatment with the lowest available dose. Combination therapy with protective agents (e.g., misoprostol or proton pump inhibitors) should be considered for these patients and also for those who are simultaneously taking low doses of aspirin or other drugs that may increase the risk of gastrointestinal events (see below and section 4.5).
Patients with a history of gastrointestinal toxicity, especially if elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding), especially in early treatment.

At any time during treatment bleeding, ulcers or gastrointestinal perforation with or without warning symptoms or previous gastrointestinal events may appear. If gastrointestinal bleeding or ulcers appear, treatment with nimesulide should be discontinued. Nimesulide should be used with caution in patients with gastrointestinal diseases, including previous peptic ulcer, gastrointestinal bleeding, ulcerative colitis or Crohn's disease.

Caution should be recommended for patients taking medications simultaneously that may increase the risk of ulceration or bleeding, like oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors (SSRIs), or antiplatelet agents such as aspirin (see section 4.5).
When there is bleeding or gastrointestinal ulceration in patients taking EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) the treatment should be discontinued.
NSAIDs should be administered with caution in patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8).

Elderly: Elderly patients have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation, which can be fatal (see section 4.2). Consequently, appropriate clinical monitoring is recommended.

Cardiovascular and cerebrovascular effects
Adequate monitoring and appropriate instructions are necessary for patients with a history of hypertension and/or mild to moderate congestive heart failure because fluid retention and oedema have been reported in association with NSAID treatment.

Clinical and epidemiological data suggest that the use of some NSAIDs (particularly at high doses and long-term treatment) may be associated with a modest increased risk of arterial thrombotic events (e.g., myocardial infarction or stroke). There is insufficient data to exclude this risk with EFRIDOL.

Patients with uncontrolled hypertension, congestive heart failure, ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease must be treated with nimesulide only after careful consideration. Similar considerations must be made before starting long-term treatment in patients with risk factors for cardiovascular disease (e.g., Hypertension, hyperlipidemia, diabetes mellitus, smoking).

Since nimesulide can interfere with platelet function, it should be used with caution in patients with bleeding diathesis (see also section 4.3). EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is not a substitute for acetylsalicylic acid for cardiovascular prophylaxis.

Renal effects
Caution should be used in the treatment of patients with renal or cardiac insufficiency with EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) as it may impair renal function. In this case, treatment should be discontinued (see also section 4.5).

Skin effects
Cases of fixed drug eruption (FDE) have been reported with nimesulide.
Treatment with nimesulide should not be resumed in patients with a history of nimesulide-related FDE (see section 4.8).
Severe 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 increased risk early in treatment: The onset of the reaction occurs in most cases within the first month of treatment. EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Effects on fertility
The use of EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) may compromise female fertility and is not recommended for women trying to get pregnant. In women who have difficulty conceiving or who are being evaluated for infertility, consider stopping treatment with EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) (see section 4.6).

EFRIDOL tablets contain lactose and therefore are not suitable for use by patients with rare hereditary galactose intolerance, LAPP lactase deficiency or glucose-galactose malabsorption.
EFRIDOL granules for oral suspension contain sucrose and are therefore not suitable for use by patients with rare hereditary fructose intolerance, glucose-galactose malabsorption, or sucrose-isomaltase deficiency.

4.5 Interactions with other medicinal products and other forms of interaction

Pharmacodynamic interactions

Other non-steroidal anti-inflammatory drugs (NSAIDs):
The simultaneous use of EFRIDOL (see section 4.4) with other non-steroidal anti-inflammatory drugs, including acetylsalicylic acid administered in anti-inflammatory doses (≥1 g as a single dose or ≥ 3 g as a daily total), is not recommended.

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

Anticoagulants
NSAIDs may enhance the effects of anticoagulants such as warfarin (see section 4.4). Patients taking warfarin or similar anticoagulant agents have a higher risk of bleeding complications when treated with EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension). Combined use is therefore not recommended (see also section 4.4) and is contraindicated in patients with severe coagulation disorders (see also section 4.3). If combined use cannot be avoided, closely monitor anticoagulant activity.

Platelet inhibitors and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

Diuretics, angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists (AIIA): NSAIDs can reduce the effect of diuretics and other antihypertensive drugs. In some patients with impaired renal function (e.g., dehydrated patients or elderly patients with decreased renal function), the simultaneous administration of an ACE inhibitor and cyclooxygenase inhibitors may increase the impairment of renal function, including the possibility of acute renal failure, which is usually reversible.

These interactions should be considered in patients who must take EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) in combination with ACE inhibitors or AIIA. Therefore, administration of these drugs in combination should be undertaken with caution, especially in the elderly. Patients must be adequately hydrated and the possibility of monitoring renal function should be considered after initiation of simultaneous treatment and subsequently on a regular basis.

Pharmacokinetic interactions: effect of nimesulide on the pharmacokinetics of other drugs
Furosemide:
In healthy subjects, nimesulide transiently reduces the effect of furosemide on the excretion of sodium and, to a lesser extent, on the excretion of potassium and reduces the diuretic response.
Co-administration of furosemide and nimesulide leads to a reduction in AUC (about 20%) and total furosemide excretion without compromising renal clearance of the latter.
Concomitant use of furosemide and EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) requires caution in patients with kidney or heart pathology, as described in section 4.4.

Lithium
It has been reported that nonsteroidal anti-inflammatory drugs reduce the clearance of lithium and this leads to high plasma levels and lithium toxicity. If EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is prescribed for a patient taking lithium, lithium levels should be closely monitored.

Potential pharmacokinetic interactions with glibenclamide, theophylline, warfarin, digoxin, cimetidine and an antacid preparation (a combination of aluminium hydroxide and magnesium) have also been studied *in vivo*. No clinically significant interactions were noted.

Nimesulide inhibits CYP2C9. The plasma concentrations of drugs that are metabolized by this enzyme may be increased if co-administered with EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension).
Caution is required when nimesulide is taken less than 24 hours before or after treatment with methotrexate because the serum levels of methotrexate may increase and thus the toxicity of this drug may be greater.
Given their effect on renal prostaglandins, prostaglandin synthetase inhibitors such as nimesulide may increase the nephrotoxicity of cyclosporines.

Pharmacokinetic interactions: Effects of other drugs on the pharmacokinetics of nimesulide

In vitro studies have shown that tolbutamide, salicylic acid and valproic acid displace nimesulide from binding sites. However, despite a possible effect on nimesulide plasma levels, these interactions were not clinically significant.

4.6 Fertility, pregnancy and lactation

The use of EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is contraindicated in the third trimester of pregnancy (see section 4.3).
As with other NSAIDs, the use of EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is not recommended in women attempting to become pregnant (see section 4.4).

Inhibition of prostaglandin synthesis may have a negative impact on pregnancy and/or developing embryo/foetus. Results of epidemiological studies suggest a higher risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of cardiac malformations was increased from less than 1% up to about 1.5%. It is believed that the risk increases with dose and duration of therapy.

In animals, the administration of prostaglandin synthesis inhibitors has been shown to cause increased pre-and post-implantation loss and embryo/foetal mortality. In addition, an increased incidence of various malformations, including cardiovascular malformation, has been reported in animals that were administered prostaglandin synthesis inhibitors during the period of organogenesis.

Studies in rabbits have shown atypical reproductive toxicity (see section 5.3) and there is no comprehensive data on the use of EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) in pregnant women. Consequently, the potential risk to humans is unknown and the prescription of the drug during the first two trimesters of pregnancy is not recommended unless absolutely necessary.

From the 20th week of pregnancy onwards, the use of Efridol may cause oligohydramnios resulting from foetal renal dysfunction. This condition may occur shortly after initiation of treatment and is usually reversible upon discontinuation of treatment. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment discontinuation. Therefore, Efridol should not be administered during the first and second trimester of pregnancy unless clearly necessary. If EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is used by a woman attempting to conceive, or during the first or second trimester of pregnancy, the dose should be kept as low as possible and the duration of treatment as short as possible. Following exposure to Efridol for several days from gestational week 20 onwards, prenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered. Efridol 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);
- the mother and neonate at the end of pregnancy to:
  - a possible prolongation of bleeding time and an anti-platelet aggregation effect which can occur even at very low doses;
  - inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently EFRIDOL 100 mg tablets (or 100 mg oral granules for suspension) are contraindicated in the third trimester of pregnancy (see sections 4.3 and 5.3).

It is not known whether nimesulide is excreted into human milk. EFRIDOL 100 mg tablets (or 100 mg granules for oral suspension) is contraindicated in women who are breastfeeding (see sections 4.3 and 5.3).

4.7 Effects on ability to drive vehicles and use machinery

There have been no studies on the ability to drive and use machines. However, patients suffering from dizziness, vertigo, or drowsiness after taking EFRIDOL should refrain from driving or operating machinery.

4.8 Side effects

a) ***Overview***

Clinical studies and epidemiological data suggest that the use of some NSAIDs (particularly at high doses and for long-term treatment) may be associated with a modest increased risk of arterial thrombotic events (e.g., myocardial infarction or stroke) (see section 4.4).

Oedema, hypertension and heart failure have been reported in association with NSAID treatment. Very rare cases of reactions involving bullous lesions including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported.

The most commonly observed adverse events are gastrointestinal. Patients may experience peptic ulcers, perforation or gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly (see section 4.4). After the administration of EFRIDOL the following have been reported: nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4). Gastritis has been observed less frequently.

b) ***Table of side effects***

The following list of side effects is based on the results of controlled clinical trials * (out of about 7,800 patients) and pharmacovigilance data. The reported cases were classified as very common (> 1/10), common (>1/100, <1/10), uncommon (>1/1,000, <1/100), rare (>1/10,000, <1/1,000) and very rare (<1/10,000), including isolated cases.

Lymphatic system disorders	Rare	Anaemia* Eosinophilia *
	Very rare	Thrombocytopenia Pancytopenia Purpura
Immune system disorders	Rare	Hypersensitivity *
	Very rare	Anaphylaxis
Disturbances of metabolism and nutrition	Rare	Hyperkalemia *
Psychiatric disorders	Rare	Anxiety * Nervousness * Nightmares *
Nervous system disorders	Uncommon	Dizziness *
	Very rare	Headache Drowsiness Encephalopathy (Reye's syndrome)
Eye disorders	Rare	Blurred vision *
	Very rare	Visual disturbances
Ear and labyrinth disorders	Very rare	Dizziness
Cardiac disorders	Rare	Tachycardia *
Vascular disorders	Uncommon	Hypertension *
	Rare	Bleeding * Fluctuations in blood pressure * Hot flashes *
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea *
	Very rare	Asthma Bronchospasm

Gastrointestinal disorders	Common	Diarrhoea * Nausea* Vomiting*
	Uncommon	Constipation * Flatulence * Gastrointestinal bleeding Duodenal ulcer and perforation Gastric ulcer and perforation
	Very rare	Gastritis * Abdominal pains Dyspepsia Stomatitis Melena Gastrointestinal bleeding Ulcer and duodenal perforation Ulcer and gastric perforation
Hepatobiliary disorders *(See section 4.4 "Special warnings and precautions for use")*	Very rare	Hepatitis Fulminant hepatitis (including fatal cases) Jaundice Cholestasis
	Common	Increased liver enzymes levels
Skin and subcutaneous tissue disorders	Uncommon	Pruritus * Eruptions * Increased sweating *
	Rare	Erythema * Dermatitis *
	Very rare	Urticaria Angioedema Facial oedema Erythema multiforme Stevens-Johnson Syndrome Toxic epidermal necrolysis
	Not known	Fixed drug eruption (see section 4.4)
Renal and urinary disorders	Rare	Dysuria * Haematuria *
	Very rare	Urinary retention * Renal insufficiency Oliguria Interstitial nephritis
Systemic disorders and conditions related to the administration site	Uncommon	Oedema *
	Rare	Malaise * Asthenia *
	Very rare	Hypothermia
Diagnostic exams	Common	Increased liver enzymes*

**Frequency data derived from clinical trials*

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 product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system at the web address http://www.aifa.gov.it/content/segnalazioni-reazioni-avverse.

4.9 Overdose

The symptoms associated with acute NSAID overdose are usually limited to drowsiness, sluggishness, nausea, vomiting and epigastric pain, generally reversible with supportive care. Gastrointestinal bleeding can occur. High blood pressure, acute renal failure, respiratory failure and coma may occur also, albeit rarely. Anaphylactic reactions have been reported after ingestion of therapeutic doses of NSAIDs and may manifest after overdose as well.

In case of overdosage with NSAIDs, patients must be managed with symptomatic and supportive treatment. There are no specific antidotes. No information is available on the elimination of nimesulide by means of haemodialysis: given its high degree of protein binding (up to 97.5%), dialysis is unlikely to be useful in the treatment of overdose. Vomiting and/or activated charcoal (60 to 100 g in adults) and/or osmotic cathartics may be indicated, if administered within 4 hours in patients with symptoms of overdose or who have taken large doses of nimesulide. Forced diuresis, alkalinisation of urine, haemodialysis or hemoperfusion may not be useful because of the high protein binding. Renal and hepatic function must be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic category: anti-inflammatory drugs/non-steroidal anti-rheumatic.
ATC code: M01AX17

Nimesulide is a nonsteroidal anti-inflammatory drug with analgesic and antipyretic effects which acts by inhibiting the enzyme cyclo-oxygenase, which synthesizes prostaglandins.

5.2 Pharmacokinetic properties

Tablets and granules for oral suspension

Nimesulide is well absorbed after oral administration. After a single dose of 100 mg of Nimesulide in adults the maximum plasma level of 3-4 mg/l is reached after 2-3 hours. AUC = 20-35 mg h/l. No statistically significant differences were found between these values and those recorded after administration of 100 mg twice daily for 7 days.

Up to 97.5% of the drug binds to plasma proteins.

Nimesulide is largely metabolised in the liver through different pathways, including the CYP2C9 isoenzymes of cytochrome P450. Therefore there is a potential drug interaction with drugs metabolized by CYP2C9 (see 4.5). The main metabolite is the para-hydroxy derivative which is also pharmacologically active. The time to appearance of the metabolite in the circulation is short (about 0.8 hours), but its formation constant is not high and is considerably lower than the nimesulide absorption constant. Hydroxynimesulide is the only metabolite found in the plasma, and is almost completely conjugated. Its half-life ranges from 3.2 to 6 hours.

Nimesulide is mainly excreted in urine (about 50% of the administered dose).
Only 1-3% is excreted as unmodified drug. Hydroxynimesulide, the main metabolite, is only found as glucuronide. Approximately 29% of the dose is excreted metabolized in faeces.

The kinetic profile of nimesulide does not change in the elderly after single and repeated doses.

In an experimental study with a single administration in patients with mild to moderate renal insufficiency (creatinine clearance 30-80 ml/min) vs. healthy volunteers, peak nimesulide plasma levels and that of its main metabolite were not higher than those of healthy volunteers. AUC and t½ beta were 50% higher, but always in

the range of variability of kinetic values observed for nimesulide in healthy volunteers. Repeated administration did not result in accumulation.
Nimesulide is contraindicated in patients with liver failure (see 4.3).

5.3 Preclinical safety data

Preclinical data reveal no particular risk for humans based on conventional pharmacology safety studies, repeated dose toxicity, genotoxicity and carcinogenic potential.
In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity.
In reproductive toxicity studies potential teratogenic or embryotoxic (skeletal malformations, dilatation of cerebral ventricles) signs were seen in rabbits, but not in rats treated up to dose levels not toxic to the mothers. Increased mortality in offspring in the immediate postnatal period and adverse effects on the fertility of rats were observed.

6. PHARMACEUTICAL INFORMATION

6.1 List of inactive ingredients

Tablets: dioctyl sodium sulfosuccinate, hydroxypropyl cellulose, lactose, sodium starch glycolate, microgranular cellulose, hydrogenated vegetable oil, magnesium stearate.
Sachets: cetomacrogol 1000, sucrose, maltodextrin, citric acid, orange flavour.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for preservation

This medicine does not require any special storage conditions

6.5 Nature and contents of container

Tablets: opaque PVC/Aluminium blister containing yellow tablets with a pre-scored centre line.

Granules for oral suspension: heat-sealed bags of laminated paper/aluminium/polythene containing free-flowing yellow granules.

6.6 Special precautions for disposal and handling

No special requirements.
Any unused product or waste materials resulting from this medicinal product should be disposed of in accordance with the requirements of local laws.

7. MARKETING AUTHORISATION HOLDER

AESCULAPIUS FARMACEUTICI S.r.l. - Via Cefalonia, 70 – 25124 Brescia, Italy.

8. MARKETING AUTHORISATION HOLDER NUMBERS

100 mg tablets – 30 tablets	MA n° 032932016
100 mg granules for oral suspension	MA n° 032932030

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Renewal date: December 2007

10. DATE OF REVISION OF THE TEXT

December 2022