SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TROCMETAM 20 mg Lyophilized Powder for Injection
Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:
Each vial contains

Tenoxicam	20 mg

Excipients:

Sodium hydroxide	3.28 mg
Sodium metabisulfite	2 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilized powder for Injection.
Yellow lyophilized cake.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TROCMETAM is indicated for the symptomatic treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis, and for the treatment of acute gouty arthritis, acute musculoskeletal pain, postoperative pain and dysmenorrhea.

4.2 Posology and method of administration

Posology / frequency and time of administration

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

For all indications except acute gout and post-operative pain, a daily dosage of 20 mg should be given at the same time of day.

For post-operative pain the recommended dose is 40 mg once daily up to five days and for acute attacks of gout the recommended dose is 40 mg once daily for two days followed by 20 mg once daily for a further five days.

In treatment of chronic disorders, the therapeutic effect of tenoxicam is evident early in treatment and there is a progressive increase in response over time. In chronic disorders, daily

doses should not exceed 20 mg. Otherwise this would increase the frequency and intensity of unwanted reactions without significantly increasing efficacy.
For patients needing long-term treatment a reduction to a daily oral dose of 10 mg may be tried for maintenance.

Method of administration:
The lyophilisate in vial should be dissolved in 2 ml of sterile water for injections provided with the medicinal product. The reconstituted solution should be used immediately through intramuscular (i.m) or intravenous (i.v) bolus injection.

When necessary treatment should be initiated with I.V. or I.M. single daily dose of 20 mg for one to two days, to be continued with the oral or rectal tenoxicam.

Lyophilized powder for injection is developed for i.m. and i.v. bolus administration; it is not recommended for use as an infusion due to the possibility of precipitation.

Additional information on special populations
Renal failure
The above dosage recommendations also apply to patients suffering from kidney disease. However, when TROCMETAM is used in patients with renal failure, careful monitoring of renal function is recommended. It should not be used in patients with severe renal impairment.

Hepatic failure
The above dosage recommendations also apply to patients suffering from liver disease. However, when TROCMETAM is used in patients with liver failure, careful monitoring of hepatic function is recommended. It should not be used in patients with severe liver impairment.

Pediatric population
No dosage recommendations have been established for children and adolescents due to insufficient data. It is not used in this age group.

Geriatric population
The elderly are at higher risk of gastrointestinal bleeding, ulceration or perforation and may have fatal consequences. In these patients, treatment should be initiated with the lowest dose and combined treatment with prophylactic drugs (e.g. misoprostol or proton pump inhibitors) should be considered for patients who simultaneously use low-dose salicylate or other drugs that increase the gastrointestinal risk (see section 4.4).

4.3 Contraindications
- TROCMETAM is contraindicated in patients with known hypersensitivity to tenoxicam or any of the excipients of TROCMETAM,
- In patients whom salicylates or other NSAIDs induce symptoms of asthma, rhinitis or

urticarial,

- In patients with active or history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy (see section 4.4)
- In patients with active, or history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of proven ulceration or bleeding) (See Section 4.4)
- In patients with severe renal, hepatic or heart failure, as with other NSAIDs,
- Treatment of perioperative pain for coronary artery bypass graft (CABG) surgery,
- During the third trimester of pregnancy.

4.4 Special warnings and precautions for use

NSAIDs inhibit renal prostaglandin synthesis and consequently may have an undesirable effect on renal haemodynamics and on salt and water balance. Prolonged use of NSAIDs may result in renal papillary necrosis and other renal dysfunction. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state. It is necessary to adequately monitor the patient with a special emphasis on cardiac and renal function (BUN, creatinine, development of oedema, weight gain, etc.) when giving TROCMETAM to patients with conditions that could increase their risk of developing renal failure, such as pre-existing renal disease, impaired renal function in diabetics, hepatic cirrhosis, congestive heart failure, volume depletion or concomitant treatment with potentially nephrotoxic medicines, diuretics and corticosteroids. This group of patients is at special risk in peri- and post-operative phases of major surgery due to the possibility of serious blood loss. They therefore require close monitoring in the post-operative and recovery periods.

Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced.

The use of Tenoxicam with concomitant NSAIDs including cyclooxygenase-2 (COX-2) selective inhibitors should be avoided.

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

TROCMETAM cannot replace corticosteroids and cannot be used to treat corticosteroid deficiency.

Gastrointestinal bleeding, ulceration and perforation

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs including TROCMETAM at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events. To date, studies have not identified any subset of patients not at risk of developing peptic ulcer and bleeding.

The elderly has an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal. Debilitated patients do not seem to tolerate ulceration or bleeding as well as others. Most of the fatal gastrointestinal events

associated with NSAIDs occurred in the elderly and/or debilitated patients. The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with hemorrhaged or perforation (see section 4.3) and in the elderly. In these patients, treatment should be initiated with the lowest dose and combined treatment with prophylactic drugs (e.g. misoprostol or proton pump inhibitors) should be considered for patients who simultaneously use low-dose salicylate or other drugs that increase the gastrointestinal risk (see below and section 4.5).

NSAIDs should be given with care to patients with a history of inflammatory bowel disease (ulcerative colitis; Crohn's disease) as their condition may be exacerbated. 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.

If peptic ulceration or gastrointestinal bleeding occurs, TROCMETAM should be withdrawn immediately.

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

Anaphylactoid reactions
As with other NSAIDs, anaphylactoid reactions may occur in patients who have not previously taken TROCMETAM. It should not be given to patients with salicylate triad (see section 4.3, section 4.4 - preexisting asthma).

Preexisting asthma
Should not be administered to patients with salicylate sensitivity and should be used with caution in patients with asthma.

Skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis (Lyell’s syndrome), have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. TROCMETAM should be discontinued at the first appearance and serious skin reactions.

Hepatic effects
The borderline abnormalities in one or more liver tests may occur in up to 15% of patients when treated with NSAIDs including TROCMETAM. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy.
Hematological Effects:

Tenoxicam inhibits platelet aggregation and may affect haemostasis. TROCMETAM has no significant influence on blood coagulation factors, coagulation time, prothrombin time or activated thromboplastin time. Patients having coagulation disorders or receiving therapy that interferes with haemostasis should, however, be carefully observed when TROCMETAM is administered. Anemia may be seen in patients using NSAIDs including TROCMETAM.

Cardiovascular and cerebrovascular effects
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and edema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that use of selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) and some NSAIDs (particularly at high doses and long term treatment) may be associated with an increased risk of thrombotic events (i.e myocardial infarction and stroke) which may increase with dose or duration of use. To minimize the potential risk, the lowest effective dose should be used for the shortest possible duration.

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

Ocular effects
Adverse eye findings have been reported with NSAIDs including Tenoxicam. Thus ophthalmic evaluation is recommended for patients who develop visual disturbances.

Antipyretic effects
As known for other anti-inflammatory medicines, TROCMETAM may mask the usual signs of infection.

Laboratory tests
NSAIDs inhibit renal prostaglandin synthesis and consequently may have an undesirable effect on renal hemodynamics and on salt and water balance. It is necessary to adequately monitor the patient with a special emphasis on cardiac and renal function (BUN, creatinine, development of edema, weight gain, etc.) when giving to patients with conditions that could increase their risk of developing renal failure, such as pre-existing renal disease, impaired renal function in diabetics, hepatic cirrhosis, congestive heart failure, volume depletion or concomitant treatment with potentially nephrotoxic drugs, diuretics and corticosteroids. This group of patients is at special risk in peri- and post-operative phases of major surgery due to possibility of serious blood loss. They therefore require close monitoring in the post-operative and recovery periods.
Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced.

This medicinal product contains less than 1 mmol (23 mg) sodium per ml, i.e it is essentially "sodium free".

This medicinal product contains sodium metabisulfite. This excipient can rarely cause severe hypersensitivity reactions and bronchospasm.

4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicyclate and salicyclates
Salicylates increase the clearance and volume of distribution of NSAIDs including tenoxicam and decrease the mean minimum steady-state plasma concentrations of tenoxicam by displacing them from protein binding sites. Concomitant use of TROCMETAM with salicylate or other NSAIDs is not recommended because of increased risk of undesirable reactions.

Gastrointestinal interactions
Caution is advised in patients using oral corticosteroid and TROCMETAM concomitantly. There is an increased risk of gastrointestinal bleeding (see section 4.4) when anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs) are combined with NSAIDs.

Methotrexate
The co-administration of some NSAIDs and methotrexate has been associated with reduced renal tubular secretion of methotrexate, higher plasma concentrations of methotrexate, and severe methotrexate toxicity. Therefore, caution should be exercised when TROCMETAM is administered concurrently with methotrexate

Zidovudine
The concomitant use of NSAIDs with zidovudine, which is used for the treatment of AIDS is associated with increased erythrocyte toxicity over the reticulocytes accompanied by severe anemia one week after starting treatment. Blood values should be monitored two weeks after starting treatment with NSAIDs.

Mifepristone
TROCMETAM should not be used for 8 – 12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.

Lithium
As TROCMETAM may decrease the renal clearance of lithium, their concomitant administration may lead to increased plasma levels and toxicity of lithium. The plasma levels of lithium should therefore be closely monitored.

Cyclosporine and Tacrolimus
As with all NSAIDs caution is advised when cyclosporine is co-administered because of the increased risk of nephrotoxicity.

Quinolones
Patients using quinolones may be at higher risk of convulsions.

Diuretics and Anti-hypertensive
As with NSAIDs in general, TROCMETAM should not be administered concurrently with potassium sparing diuretics. There is a known interaction between these two classes of compounds, which may cause hyperkaliemia and renal failure.

No clinically significant interaction between Tenoxicam and furosemide was noted. But TROCMETAM attenuates the blood pressure lowering effect of hydrochlorothiazide. As known from other NSAIDs, TROCMETAM might attenuate the antihypertensive effects of alpha-adrenergic blockers, beta-adrenergic blockers and ACE-inhibitors.

No interactions have been reported between Tenoxicam and centrally acting alpha agonists or calcium channel blockers.

There was no clinically relevant interaction when Tenoxicam was administered together with atenolol.

During clinical trials no interaction was reported for patients treated concomitantly with digitalis products. Thus concurrent dosing of TROCMETAM and digoxin appears to be without major risk.

Antacids and H2-receptor antagonists
No clinically relevant interaction has been found with concomitantly administered antacids and cimetidine at the recommended dosages.

Probenecid
Co-administration of probenecid and tenoxicam treatment may increase plasma concentration of tenoxicam. The clinical significance of this observation has not been established.

Anticoagulants
No clinically relevant interaction has been found with concomitantly administered warfarin and phenprocoumon, and low molecular weight heparin at the recommended dosages. Nevertheless, as for other NSAIDs, careful monitoring is recommended when patients concomitantly receive anticoagulants.

Oral antidiabetics
The clinical effect of the oral antidiabetic medicines glibornuride, glibenclamide and tolbutamide was not modified by Tenoxicam. Nevertheless, as for other NSAIDs, careful monitoring is recommended when patients concomitantly receive oral antidiabetic drugs.

Alcohol
Gastric mucosal damage is greater when tenoxicam is taken with alcohol.

No clinically relevant interaction was found in small numbers of patients receiving Tenoxicam with penicillamine or parenteral gold.

4.6 Pregnancy and lactation

General recommendation

Pregnancy category: C/D (3rd trimester)

Women with childbearing potential / Contraception

No information on the effects of TROCMETAM on contraception is available. The use of tenoxicam, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. If TROCMETAM is used by a woman attempting to conceive, the dose should be kept as low and duration of treatment as short as possible. TROCMETAM is contraindicated during the third trimester of pregnancy.

Pregnancy

No clinical data is available on the exposure to tenoxicam during pregnancy (see section 5.3). Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development (See section 5.3).

Caution should be exercised when TROCMETAM is given to pregnant women.
NSAIDs have an inhibitory effect on the synthesis of prostaglandins, and this effect can lead to the closure of the fetal ductus arteriosus when the drug is administered in the final trimester of pregnancy and to delay parturition by prolonging delivery. Treatment with TROCMETAM should be avoided in the third trimester of pregnancy.

Lactation

Based on findings from single dose administration, a very small amount (mean value less than 0.3% of the dose) of tenoxicam passes into breast milk (see section 5.2).

There is no evidence of adverse reactions in breast-fed infants of mothers taking Tenoxicam, however, a possible side effect should not be disregarded and in case of suspicion, infants should be weaned or the drug discontinued.

Reproduction ability/Fertility

The use of tenoxicam, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of tenoxicam should be considered (See section 5.3).

4.7 Effects on ability to drive and use machines

Patients experiencing adverse events that might affect driving or using machines, such as vertigo, dizziness or visual disturbances should refrain from driving a car or using machines.

4.8 Undesirable effects

Based on clinical trials including large numbers of patients, Tenoxicam proved to be well tolerated in the recommended dose. Usually the undesirable effects reported were mild and transient. In a small proportion of patients the interruption of treatment due to undesirable effects was necessary. The local tolerance of the parenteral administration of Tenoxicam was found to be good.

The following terms and frequency ratings are used for the undesirable effects associated with the use of Tenoxicam.

Very common (≥ 1/10); Common (≥ 1/100 to < 1/10); Uncommon (≥ 1/1.000 to < 1/100); Rare (≥ 1/10.000 to < 1/1.000); Very rare (< 1/10.000); Not known (cannot be estimated from the available data)

Blood and lymphatic system disorders

Not known: Anemia, agranulocytosis, leucopenia, thrombocytopenia

Immune system disorders

Not known: Hypersensitivity reactions such as dyspnea, asthma, anaphylactic reactions, angioedema

Metabolism and nutrition disorders

Uncommon: Loss of appetite

Psychiatric disorders

Uncommon: Sleep disorders

Nervous system disorders

Common: Dizziness, headache

Eye disorders

Not known: Problems with vision

Ear and Labyrinth Disorders

Uncommon: Vertigo

Cardiac disorders

Uncommon: Palpitation

Not known: Heart failure

Vascular disorders

Not known: Vasculitis Clinical trial and epidemiological data suggest that use of selective cyclooxygenase-2 inhibitors (COX-2 Inhibitors some NSAIDs (particularly at high doses and long term treatment) may be associated with an increased risk of thrombotic events (i.e myocardial infarction and stroke) which may increase with dose or duration of use.

Although tenoxicam has not shown to increase thrombotic events such as myocardial infarction, there are insufficient data to exclude such a risk with tenoxicam.

Gastrointestinal disorders
Common: Gastric, epigastric and abdominal pain, dyspepsia, nausea, epigastric burning, gastrointestinal perforation
Uncommon: Gastrointestinal haemorrhages including haematemesis and melena, ulcers, constipation, diarrhea, stomatitis, gastritis, vomiting, dry mouth
Not known: Exacerbation of colitis and Crohn's disease were reported following administration.

Hepatobiliary disorders
Not known: Hepatitis

Skin and subcutaneous tissue disorders
Uncommon: Pruritus (in the anal region after rectal administration), erythema, exanthema, rash, urticaria
Very rare: Stevens Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), photosensitivity reaction

Pregnancy, pueperium conditions and perinatal diseases
Not known: Isolated cases of female infertility have been reported with drugs known to inhibit cyclooxygenase / prostaglandin synthesis, including tenoxicam.

General disorders and administration site conditions
Uncommon: Fatigue, oedema

Investigations
Uncommon: Increased hepatic enzymes, increased blood urea (BUN) or creatinine
Not known: Increase in blood pressure, especially in patients treated with cardiovascular drugs

Post-marketing data
Safety profile in post-marketing experience complies with the clinical studies.

4.9 Overdose and therapy
Symptoms
Although there is no experience with acute overdose with Tenoxicam, the undesirable effects given in Section 4.8 can be expected to be more prominent.

Gastrointestinal bleeding may occur. Hypertension, acute renal failure, respiratory depression and coma may occur rarely following the administration of NSAIDs. Anaphylactic reactions have been reported in the therapeutic use of NSAIDs, and these reactions may occur after overdose.

Treatment
There is no known antidote for TROCMETAM. However, in case overdose with TROCMETAM, symptomatic treatment and supportive treatment such as absorption reduction (i.e. Gastric lavage or activated charcoal) and excretion catalyst should be administered. Dialysis does not significantly clear NSAIDs from the blood stream.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Non-steroidal anti-inflammatory and antirheumatic products (Oxicams)
ATC Code: M01AC02

The active ingredient of TROCMETAM, tenoxicam, is a non-steroid anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic, antipyretic properties and it also inhibits platelet aggregation. Tenoxicam inhibits prostaglandin biosynthesis both in vitro and in vivo. In vitro investigation on cyclo-oxygenase (COX) isoenzymes prepared from human COS-7 cells have shown that tenoxicam inhibits COX-1 and COX-2 isoenzymes approximately to the same extent i.e. COX-2/COX-1 ratio equals to 1.34.

In-vitro tests of leukocyte peroxidase suggest that tenoxicam may act as a scavenger for active oxygen at the site of inflammation.

Tenoxicam is a potent in-vitro inhibitor of human metalloproteinases (stromelysin and collagenase) which induce cartilage breakdown. These pharmacological effects explain, at least in part, the therapeutic benefit of Tenoxicam in the treatment of painful inflammatory and degenerative disorders of the musculoskeletal system.

5.2 Pharmacokinetic properties
General properties:
Absorption
After intramuscular administration, its bioavailability is complete and is not different than oral administration. Following intramuscular injection levels at or above 90% of the maximally achieved concentrations are reached as early as 15 minutes after a dose.
With the recommended dosage regimen of 20 mg once daily, steady-state plasma concentrations are reached within 10-15 days, with no unexpected accumulation. The average concentration at steady state is 11 mg/L when given at 20 mg once daily and this does not change even on treatment for up to four years.
As predictable from single dose kinetic, plasma concentrations at steady state are 6-fold higher than those reached after a single dose.

Distribution:
During the first two hours following intravenous administration, plasma levels of tenoxicam decline rapidly. After this short period, no differences in plasma concentrations between intravenous and oral dosing are seen. The mean volume of distribution at steady state is 10 to 12 L.
In the blood over 99% of the drug is bound to albumin. Tenoxicam penetrates well into the synovial fluid.
Peak concentrations are reached later than in plasma.
Based on findings from single dose administration, a very small amount (mean value less than 0.3% of the dose) of tenoxicam passes into breast milk (see section 4.6).

Biotransformation:
Tenoxicam is excreted after virtually complete biotransformation to pharmacologically inactive metabolites.

Elimination:
Up to two thirds of an oral dose is excreted in the urine (mainly as the inactive 5'-hydroxytenoxicam) and the rest via the bile (a significant portion in the form of glucuronidated compounds). Less than 1% of the administered dose is recovered in the urine in form of the parent compound. The mean elimination half-life of tenoxicam is 72 hours (range 59 to 74 hours). The total plasma clearance is 2 mL/min.

Linearity / Non-linearity:
The pharmacokinetics of tenoxicam are linear in the investigated dose range of 10 to 100 mg.

Special Populations
Renal failure:
Studies in patients with renal insufficiency suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those seen in healthy subjects.

Hepatic failure:
Studies in patients with liver insufficiency suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those seen in healthy subjects.

Elderly:
Studies in the elderly suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those seen in healthy subjects. The elderly show the same kinetics profile as healthy volunteers.

Other:
Patients with rheumatic diseases show the same kinetics profile as healthy volunteers.
Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced (see section 4.4)

5.3 Preclinical safety data

Carcinogenicity

Tenoxicam showed no carcinogenic effects in animals.

Mutagenicity

Tenoxicam showed no mutagenic effects in animals.

Impairment of fertility

The use of tenoxicam, as with any drug known to inhibit cyclooxygenase/ prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, discontinuation of tenoxicam should be considered.

Teratogenicity

Tenoxicam showed no teratogenic effects in rats.

6. PHARMACEUTICAL PROPERTIES

6.1 List of Excipients

Mannitol
Sodium hydroxide
Trometamol
Sodium metabisulfite
Disodium EDTA
Water for injection
Sodium hydroxide and/or hydrochloric acid for pH adjustment

6.2 Incompatibilities

Do not use TROCMETAM lyophilisate for solution for injection with infusions because of the possibility of precipitation.

6.3 Shelf Life

24 months

6.4 Special precautions for storage

Store at temperature below 25ºC, out of reach of children and in the original packaging. Use immediately after reconstitution.

6.5 Nature and contents of container

Each packaging contains 1 vial and 1 ampoule.
Vial: Colorless Type I glass vial sealed with bromobutyl rubber stopper and flip-off cap.
Ampoule: Colorless, type I glass ampoule

6.6 Special precautions for disposal and other handling

The unused products and waste materials must be destructed according to the local

regulations.

Shake/swirl until product is completely dissolved during reconstitution.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

2018/371

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first approval: 13.07.2018
Date of renewal of the approval: -

10. DATE OF REVISION OF THE TEXT

14.04.2020