SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

Flokort 1 mg/ml + 3 mg/ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contain 1 mg of dexamethasone phosphate (equivalent to 1.09 mg of dexamethasone sodium phosphate) and 3 mg of ofloxacin.

Excipient(s) with known effect:
Each ml of eye drops, solution contains 0.2 mg of benzalkonium chloride (50% solution).
Each ml of eye drops, solution contains 4.0 mg of phosphate buffers (as sodium dihydrogen phosphate monohydrate and di-sodium hydrogen phosphate dodecahydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution,
Clear, colourless or lightly yellow solution, with pH between 6.5 and 7.2 and osmolality between 280 and 320 mOsm/kg.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Flokort is indicated in pre and post operatory of eye surgeries when infection and inflammation may exist in simultaneous or in the treatment of infections of the external surface of the eye by ofloxacin sensitive microorganisms (see sections 4.4 and 5.1), meaning bacterial infections with a severe inflammatory reaction.

Flokort is indicated in adults (including the elderly).

4.2. Posology and method of administration

Flokort is intended for topical ocular use only.

Posology
Adults
Apply one to two drops in the affected eye(s), three to six times a day
Duration of the treatment should not be longer than 10 days.

Elderly
There is extensive experience in the use of dexamethasone eye drops in elderly patients. The posology recommendations above take into consideration the clinical data resulting from this experience.

Paediatric population
The safety and efficacy of Flokort in the paediatric population is not established.
Flokort should be used with precaution in children and adolescents.
In children, continued long-term corticosteroid therapy should be avoided due to possibility of adrenal suppression (see section4.4).
The safety and efficacy of ofloxacin in children aged less than one year old were not established. No data is available on the safety and efficacy in children aged less than 2 years old for dexamethasone.
Current available data are described in sections 4.8, 5.1 and 5.2, however no posology recommendation can be established.

Liver and kidney failure patients
No dosage adjustment required.

In order to avoid contamination of the dropper container and of the solution, caution should be taken not to touch the dropper container on the eyelids, surrounding areas or other surfaces. Keep the bottle tightly closed when not in use.

To reduce possible systemic absorption, compression of the lacrimal sac is recommended in the inner corner of the eye (nasolacrimal occlusion), for 2 minutes. This should be performed after the instillation of each drop.

Method of administration:
Always wash the hands before putting the drops in the eye(s).
1. To open the bottle, unscrew the cap by turning in a counter clockwise direction;
2. Tilt your head back and pull your lower eyelid down slightly to form a pocket between your eyelid and eye.
3. Invert the bottle and press lightly until a single drop is dispensed into the eye as directed by your doctor. Do not touch your eye or eyelid with the dropper insert.
4. Close the eye and press a finger into the corner of the eye by the nose for about 2 minutes. This avoids the medicine to be spread to other parts of the body.
5. Repeat steps 2 to 4 with the other eye if instructed to do so by your doctor.
6. Replace the cap by turning it until it is firmly touching the bottle. Do not overtighten the cap.

4.3. Contraindications
- Hypersensitivity to ofloxacin, other quinolones or to any of the excipients listed in section 6.1;
- Acute purulent bacterial infection, including infections caused by Pseudomonas and micobacteria infections;
- Fungal infections;
- Epithelial keratitis caused by Herpes simplex (dendritic keratitis), vaccinia, varicela zoster and the majority of other viral infections of the cornea and of the conjunctiva;
- Amoebic keratitis;
- Perforation, ulceration and lesions of the cornea with incomplete epithelization (se also section 4.4);
- Known glucocorticoid induced ocular hypertension

4.4. Special warnings and precautions for use
Flokort is an association of two active substances that combines anti-inflammatory and antiallergic action of dexamethasone with a large spectrum bactericidal effect of ofloxacin.

Flokort is intended for topical ocular use only.

Dexamethasone

Topical steroids should never be applied in eyes that show undiagnosed redness.

Patients should be monitored in frequent intervals during treatment with eye drops containing dexamethasone. Long-term treatment with corticosteroids may cause ocular hypertension/glaucoma (particularly in patients with intraocular pressure previously induced by steroids or with pre-existing high intraocular pressure or glaucoma) and may also originate cataract formation, especially in children and elderly population.

Use of corticosteroids may also cause opportunistic eye infections due to suppression of host response or wound healing delay. Additionally, topical ocular corticosteroids may promote, worsen or mask signs and symptoms of opportunistic eye infections.

Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral and fungal infections and mask the clinical signs of infections, preventing recognition of ineffectiveness of the antibiotic. In such cases antibiotic therapy is mandatory. Fungal infection should be suspected in patients with persistent corneal ulceration who have been or are receiving these drugs, and corticosteroids therapy should be discontinued if fungal infection occurs.

Patients with eye infection should only be treated with a topical steroid when infection is controlled with an effective anti-infectious treatment. Patients should be carefully and regularly monitored by an ophthalmologist.

In some inflammatory diseases, such as episcleritis, systemic non-steroid anti-inflammatories (NSAID) are the first line of treatment. Dexamethasone should only be used if NSAIDs are contraindicated.

Generally, patients with corneal ulcer should not be treated with topical dexamethasone, except in the cases where the inflammatory process is the main cause for delayed wound healing and where appropriate etiological treatment is already prescribed. These patients should be carefully and regularly monitored by an ophthalmologist.
Decreased thickness of the cornea and sclera may increase the risk of perforation with the use of topical corticosteroids.

Corneal calcification that require corneal graft surgery for vision rehabilitee have been reported in patients treated with ophthalmic formulations containing phosphates, such as Flokort. At first signs of corneal calcification, the medicine should stop to be used and switch to medicine without phosphates.

In children, continued long-term corticosteroid therapy should be avoided due to possible adrenal, suppression.

Posterior subcapsular cataracts may occur in cumulative doses of dexamethasone.

Diabetic patients may present increased probability for developing subcapsular cataracts following application of topical steroids.

Use of topical steroids in allergic conjunctivitis is only recommended in severe forms of allergic conjunctivitis unresponsive to standard therapy and for a short period of time.

Cushing’s syndrome and/or adrenal suppression associated with systemic absorption of ocular dexamethasone may occur after intensive or long-term continuous therapy in predisposed patients, including

children and patients treated with CYP3A4 inhibitors (including ritonavir and cobicistat). In these cases, treatment should be progressively discontinued.

Use of contact lenses should be avoided during treatment with eye drops with corticosteroids due to increased risk of infection.

Visual disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as persistent blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Ofloxacin
Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions, some following the first dose, have been reported in patients receiving systemic quinolones, including ofloxacin. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), airway obstruction, dyspnoea, urticaria, and itching.

If an allergic reaction to Flokort occurs, discontinue the drug. Use Flokort with caution in patients who have exhibited sensitivities to other quinolones antibacterial agents.

When using Flokort the risk of rhinopharyngeal passage which can contribute to the occurrence and the diffusion of bacterial resistance should be considered. As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms.

If worsening infection occurs, or if clinical improvement is not noted within a reasonable period (2 to 3 days), the patient should be re-evaluated by the ophthalmologist and alternative therapy considered.

Cardiac disorders
Caution should be taken when using fluoroquinolones, including Flokort in patients with known risk factors for prolongation of the QT interval such as, for example:
- congenital long QT syndrome
- concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics)
- uncorrected electrolyte imbalance (e.g. hypokalaemia, hypomagnesaemia)
- cardiac disease (e.g. heart failure, myocardial infarction, bradycardia) (see section 4.2 Elderly, section 4.5, section 4.8, section 4.9).

Elderly patients and women may be more sensitive to QTc-prolonging medications. Therefore, caution should be taken when using fluoroquinolones, including Flokort, in these populations.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including levofloxacin, particularly in older patients and those treated concurrently with corticosteroids. Therefore, caution should be exercised and treatment with Flokort should be discontinued at the first sign of tendon inflammation (see section 4.8).

Use Flokort with caution in patients who have exhibited sensitivities to other quinolone antibacterial agents. Data are not sufficient to establish efficacy and safety of Flokort in the treatment of conjunctivitis in neonates.

The use of Flokort in neonates with ophthalmia neonatorum caused by Neisseria gonorrhoeae or Chlamydia trachomatis is not recommended as it has not been evaluated in such patients.

Use in elderly: No comparative data are available with topical dosing in elderly versus other age groups.

Clinical and non-clinical publications have reported the occurrence of corneal perforation in patients with pre-existing corneal epithelial defect or corneal ulcer, when treated with topical fluoroquinolone antibiotics. However, significant confounding factors were involved in many of these reports, including advanced age, presence of large ulcers, concomitant ocular conditions (e.g. severe dry eye), systemic inflammatory diseases (e.g. rheumatoid arthritis), and concomitant use of ocular steroids or non-steroidal anti-inflammatory drugs. Nevertheless, it is necessary to advise caution regarding the risk of corneal perforation when using product to treat patients with corneal epithelial defects or corneal ulcers.

Corneal precipitates have been reported during treatment with topical ophthalmic ofloxacin. However, a causal relationship has not been established.

Long-term, high dose use of other fluoroquinolones in experimental animals has caused lenticular opacities. However, this effect has not been reported in human patients, nor has it been noted following topical ophthalmic treatment with ofloxacin for up to six months in animal studies including studies in monkeys.

Sun or UV-exposition should be avoided during use of Flokort due to the potential for photosensitivity.

Use of contact lenses is not recommended in patients receiving treatment for an eye infection.

Flokort contains benzalkonium chloride
This medicine contains 0.1 benzalkonium chloride in each ml of solution.
Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. Remove contact lenses before using this medicine and put them back 15 minutes afterwards.
Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

Flokort contains phosphate buffers
This medicinal product contains 4.0 mg of phosphates in each ml of solution. See section 4.8.

4.5. Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed.

If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 15 minutes apart. Eye ointments should be administered last.

Calcium phosphate precipitates have been reported on the corneal stroma surface when corticosteroid and topical beta-blockers were used at the same time.

It has been shown that the systemic administration of some quinolones inhibits the metabolic clearance of caffeine and theophylline. Drug interaction studies conducted with systemic ofloxacin have demonstrated that metabolic clearance of caffeine and theophylline are not significantly affected by ofloxacin.

Although there have been reports of an increased prevalence of CNS toxicity with systemic dosing of fluoroquinolones when used concomitantly with systemic nonsteroidal anti-inflammatory drugs (NSAIDs), this has not been reported with the concomitant systemic use of NSAIDs and ofloxacin.

Like other fluoroquinolones, Flokort should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics) (see section 4.4).

The risk of increased intraocular pressure associated with prolonged corticosteroid therapy may be more likely to occur with concomitant use of anticholinergics, especially atropine and related compounds, in patients predisposed to acute angle closure.

CYP3A4 inhibitors (including ritanovir and cobicistat) may decrease dexamethasone clearance resulting in increased effects and adrenal suppression/Cushing's syndrome. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid effects.

The following drug interactions are possible, but are unlikely to be of clinical significance, following the use of Flokort:
- The therapeutic efficacy of dexamethasone may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin.
- Glucocorticoids may increase the need for salicylates as plasma salicylate clearance is increased.

4.6. Fertility, pregnancy and lactation

Pregnancy
There are no sufficient amount of data from the use of Flokort in pregnant women to assess the possible occurrence of harmful effects.
Corticosteroids cross the placenta. Teratogenic effects were observed in animals (see section 5.3). However, there is no evidence up to date of inducing teratogenic effect in humans. Following systemic administration of high doses of corticosteroids, effects on the foetus/new-born were reported (inhibition of intrauterine growth, inhibition of adrenal cortex function). These effects were not reported with ocular use.
There are no or limited amount of data on the use of dexamethasone eye drops during pregnancy. Studies in animals have shown that topically applied steroids can be absorbed systemically and can cause abnormalities of foetal development in pregnant animals (see section 5.3). Although the relevance of these findings to human beings has not been established, the use of Flokort during pregnancy should be avoided.
Ofloxacin crosses the placenta and is distributed in the amniotic liquid in humans. Systemic administration of quinolones may cause arthropathy in young animals. As precautionary measure, use of Flokort should be avoided during pregnancy.

Breastfeeding
Because ofloxacin and other quinolones taken systemically are excreted in breast milk, and there is potential for harm to nursing infants, a decision should be made whether to temporarily discontinue nursing or not to administer the drug, taking into account the importance of the drug to the mother.
Systemically administered corticosteroids appear in human milk in quantities that could affect the child being breastfed. However, when instilled topically, systemic exposure is low. It is unknown whether dexamethasone is excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the mother.

Fertility
There is no data on potential effects of Flokort on fertility.

4.7. Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.
Like other eye drops, the vision may be temporarily blurred, which may affect the ability to drive or use machines. In case of blurred vision, patients should not drive or operate hazardous machinery until vision is clear.

4.8. Undesirable effects
Undesirable effects are listed in table below by system organ class and frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing frequency. The frequencies are defined as follows: 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) and not known (cannot be estimated from the available data).

System organ class	Frequency	Undesirable effect
Immune System Disorders	Not known	Hypersensitivity reaction including signs or symptoms of eye allergy (such as eye pruritus and eyelid pruritus) and anaphylactic reactions (such as angioedema, dyspnea, anaphylactic shock, oropharyngeal swelling, facial oedema and tongue swollen)
Nervous System Disorders	Not known	Dizziness
Eye disorders	Very common	Increased intraocular pressure
	Common	Eye irritation, ocular discomfort, burning, eye pruritus, prickling sensation and blurred vision. (these symptoms are mild and transient with no consequences)
	Uncommon	Delayed wound healing, posterior capsular cataract, opportunistic infections and glaucoma
	Very rare	Mydriasis, facial oedema, ptosis, corticosteroid induced uveitis, corneal calcifications, lens keratopathy, change in cornea thickness (thinning), corneal oedema, cornea perforation, conjunctivitis, keratitis
	Not known	Blurred vision (see section 4.4), photophobia, eye oedema, foreign body sensation, tearing, dry eye, eye pain, ocular hyperaemia, periorbital oedema (including eyelid oedema)
Cardiac disorders	Not known	Ventricular arrhythmia and

		torsades de pointes (reported predominantly in patients with risk factors for QT prolongation); ECG QT prolonged
Gastrointestinal Disorders	Not known	Nausea
Skin and Subcutaneous Tissue Disorders	Not known	Stevens-Johnson syndrome, Toxic epidermal necrolysis
Endocrine disorders	Not known	Cushing's syndrome, adrenal suppression (see section 4.4)

see section "Description of selected undesirable effects"

Ruptures of the shoulder, hand, Achilles, or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving systemic fluoroquinolones. Studies and post marketing experience with systemic quinolones indicate that a risk of these ruptures may be increased in patients receiving corticosteroids, especially geriatric patients and in tendons under high stress, including Achilles tendon (see section 4.4).

Description of selected undesirable effects
Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas. Due to the steroid component, in diseases causing thinning of the cornea or sclera, there is a higher risk for perforation especially after topical long treatments.

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.

4.9. Overdose
In the event of topical overdose, treatment should stop. In case of prolonged irritation, wash the eyes with sterile water.
In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.
Symptoms due to accidental ingestion are not known. However, like with other corticosteroids, the doctor should consider a gastric lavage or emesis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Ophtalmologicals. Antiinflammatory agents and antiinfectives in combination. Coritcosteroids and antiinfectives in combination.
ATC code: S01CA01

Flokort is an association of two active substances that combines anti-inflammatory and antiallergic action of dexamethasone with a large spectrum bactericidal effect of ofloxacin.

Dexamethasone
Dexamethasone sodium phosphate is a soluble inorganic ester of dexamethasone. It is a synthetic corticosteroid with anti-inflammatory and antiallergic effects. Dexamethasone is a highly potent and long-

acting glucocorticoid. It has greater anti-inflammatory potency than hydrocortisone (aproximately 25:1) iy than prednisolone (5:1).
The actions of corticosteroids are mediated by the binding of the corticosteroid molecules to receptor molecules located within sensitive cells. Corticosteroid receptors are present in human trabecular meshwork cells and in rabbit iris ciliary body tissue.

Corticosteroids inhibit phospholipase A2 thereby preventing the generation of substances which mediate inflammation, for example, prostaglandins. Corticosteroids also produce a marked, though transient, lymphocytopaenia. This depletion is due to redistribution of the cells, the T lymphocytes being affected to a greater degree than the B lymphocytes. Lymphokine production is reduced, as is the sensitivity of macrophages to activation by lymphokines. Corticosteroids also delay epithelial regeneration, diminish post-inflammatory neo- vascularisation and reduce towards normal levels the excessive permeability of inflamed capillaries.
The actions of corticosteroids described above are exhibited by dexamethasone and they all contribute to its anti-inflammatory effect.

Ofloxacin
Ofloxacin is a synthetic fluorinated 4-quinolone antibacterial agent with activity against a broad spectrum of Gram negative and to a lesser degree Gram positive organisms.
Ofloxacin has been shown to be active against most strains of the following organisms both in vitro and clinically in ophthalmic infections. Clinical trial evidence of the efficacy of ofloxacin against S. pneumoniae was based on a limited number of isolates.
Gram-negative bacteria: Acinetobacter calcoaceticus var. anitratum, and A. calcoaceticus var. iwoffi; Enterobacter Sp. including E. cloacae; Haemophilis Sp, including H. influenza and H. aegyptius; Klebsiella Sp., including K. Pneumoniae; Moraxella Sp., Morganella morganii; Proteus Sp., including P. Mirabilis; Pseudomonas Sp.; including P. Aeruginosa, P. cepacia, and P. fluoroscens; and Serratia Sp., including S. marcescens.
Gram-positive bacteria: Bacillus Sp.; Corynebacterium Sp.; Micrococcus Sp.; Staphylococcus Sp., including S. aureus and S. epidermidis; Streptococcus Sp., including S. Pneumoniae, S. viridans and Beta-haemolytic.
The primary mechanisms of action is through inhibition of bacterial DNA gyrase, the enzyme responsible for maintaining the structure of DNA.
Ofloxacin is not subject to degradation by beta-lactamase enzymes nor is it modified by enzymes such as aminoglycoside adenylases or phosphorylases, or chloramphenicol acetyltransferase.

5.2. Pharmacokinetic properties

Dexamethasone
Absorption
Due to its hydrophilic properties, dexamethasone sodium phosphate is poorly absorbed by intact corneal epithelium.
Following ocular route absorption and through nasal mucosa, dexamethasone sodium phosphate is hydrolized by the enzymes in the tear film and cornea to a lipophilic compound that easily penetrates the intact corneal epithelium.
When given topically to the eye, dexamethasone is absorbed into the aqueous humour, cornea, iris, choroid, ciliary body and retina. Peak corneal and aqueous humour levels are reached after 1-2 hours. Systemic absorption occurs but may be significant only at higher dosages or in extended paediatric therapy.

Distribution

Tissue distribution studies in animals show a high uptake of dexamethasone by the liver, kidney and adrenal glands; a volume of distribution has been quoted as 0.58 l/kg. In man, over 60% of circulating steroids are excreted in the urine within 24 hours, largely as unconjugated steroid.

Biotransformation
Following ocular route absorption and through nasal mucosa, dexamethasone sodium phosphate is hydrolized to dexamethasone.
Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation. Up to 77% of dexamethasone is bound to plasma proteins, mainly albumin. This percentage, unlike cortisol, remains practically unchanged with increasing steroid concentrations. The mean plasma half life of dexamethasone is 3.6 ± 0.9h.

Elimination
Dexamethasone also appears to be cleared more rapidly from the circulation of the foetus and neonate than in the mother; plasma dexamethasone levels in the foetus and the mother have been found in the ratio of 0.32:1. Dexamethasone and its metabolites are predominatly eliminated through the kidneys.

Ofloxacin
Absorption
After ophthalmic instillation, ofloxacin is well maintained in the tear-film.
In healthy voluteers
The systemic absorption of ofloxacin after topical administration is not well established; however, the seric concentrations after topical administration are minimal, with a reduced potential to cause side effects.

Distribution
The distribution of ofloxacin on human eye tissue and fluids is not well characterised.
Ofloxacin crosses the placental barrier and is distributed in the amniotic liquid.
Ofloxacin is also distributed in breast milk.
Half-life:
The half-life on the tear film is 3 to 4 hours.

Biotransformation
Less than 10% is metabolised as inactive metabolites.

Elimination
Renal route: 95% intact and 5% as metabolites; eliminaiton half-life between 4 and 8 hours.
Fecal route: 4 to 8 %.

5.3. Preclinical safety data
Quinolones, including ofloxacin, have caused arthropathy in immature animals of several species when administered systemically. However, there was no evidence of toxicity in animals after topical administration at a concentration of 0.3 mg/ml.
Some mutagenicity tests suggest a possible potential for DNA damage. No carcinogenicity tests have been performed, up to date.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Sodium chloride

Benzalkonium chloride (50% solution)
Sodium dihydrogen phosphate monohydrate
Di-sodium hydrogen phosphate dodecahydrate
Water for injections
Hydrochloric acid or sodium hydroxide for pH adjustment

6.2. Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life
2 years.
After first opening: 28 days.

6.4. Special precautions for storage
Do not store above 25ºC.

6.5. Nature and contents of container
Low-density polyethylene (LDPE) bottle with high-density polyethylene (HDPE) closing cap and low-density polyethylene (LDPE) dropper insert.
The bottle contains 5 ml of solution.

6.6. Special precautions for disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Laboratório Edol - Produtos Farmacêuticos, S.A.
Av. 25 de Abril, 6-6A
2795-225 Linda–a-Velha
Portugal

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

07/2019