Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

UKPAR

Oftaquix® Unit Dose 5 mg/ml eye drops in single-dose container (levofloxacin hemihydrate)

UK/H/0464/002/MR

UK Licence Number: PL 16058/0007

Applicant: Santen Oy

LAY SUMMARY

Oftaquix® Unit Dose 5 mg/ml eye drops in single-dose container
(levofloxacin hemihydrate)

This is a summary of the Public Assessment Report (PAR) for Oftaquix® Unit Dose 5 mg/ml eye drops in single-dose container (PL 16058/0007). It explains how Oftaquix® Unit Dose 5 mg/ml eye drops in single-dose container were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Oftaquix Unit Dose 5 mg/ml Eye Drops.

This medicinal product will be referred to as Oftaquix eye drops in the remainder of the Lay Summary for ease of reading.

For practical information about using Oftaquix eye drops, patients should read the package leaflet or contact their doctor or pharmacist.

What are Oftaquix eye drops and what are they used for?
Oftaquix eye drops contain the active ingredient levofloxacin hemihydrate. It is used to treat bacterial infections that affect the front surfaces of the eye in adults and children aged 1 year and over. One type of infection in this area is called bacterial conjunctivitis, which is an infection of the covering of the front of the eye (conjunctiva).

It is not recommended for children aged below 1 year.

How are Oftaquix eye drops used?
Oftaquix eye drops are for ocular use and have to be applied to the outer surface of the eye.

The recommended dose is as follows:
Days 1 - 2
- Use one to two drops in the affected eye(s) every 2 hours.
- Use a maximum of eight times per day.

Days 3 - 5
- Use one to two drops in the affected eye(s).
- Use a maximum of four times per day.

In elderly patients, no adjustment of the recommended dose is required. The usual total treatment course is 5 days. The patient's doctor will advise how long to apply the drops for. If the patient is putting any other medicine in their eye, he or she should wait at least 15 minutes between applying the different types of drops.

Please read Section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

This medicine can only be obtained with a prescription.

How do Oftaquix eye drops work?
Levofloxacin hemihydrate is an antibiotic of the type called fluoroquinolones (sometimes shortened to quinolones). It works by killing some types of bacteria that can cause infections.

How have Oftaquix eye drops been studied?
Oftaquix eye drops is a new formula of an existing product, the preserved product Oftaquix 5 mg/ml eye drops, and as such the data to support this application are primarily based on the data submitted for this

existing product. Apart from data from two pharmacokinetic studies, no new data were submitted or were required.

What are the possible side effects from Oftaquix eye drops?
For information about side effects that may occur when using Oftaquix eye drops, please refer to Section 4 of the package leaflet or the Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

Why are Oftaquix eye drops approved?
No new or unexpected safety concerns arose from this application. It was, therefore, considered that the benefits of Oftaquix eye drops outweigh the identified risks, and the grant of a Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Oftaquix eye drops?
A Risk Management Plan has been developed to ensure that Oftaquix eye drops are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Oftaquix eye drops, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Oftaquix eye drops.
A Marketing Authorisation was granted in the UK on 21 June 2006.

Following a mutual recognition procedure that concluded on 30 April 2007, Denmark, Finland, Germany, Iceland, Italy and Sweden also agreed to grant a product licence for Oftaquix® Unit Dose 5 mg/ml eye drops in single-dose container (UK/H/0464/002/MR).

The full PAR for Oftaquix eye drops follows this summary.

For more information about treatment with Oftaquix eye drops, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in September 2017.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Santen Oy a Marketing Authorisation for the medicinal product Oftaquix Unit Dose 5 mg/ml Eye Drops (PL 16058/0007). The product is a prescription-only medicine (POM) and is indicated for the topical treatment of bacterial external ocular infections in patients ≥1 year of age caused by levofloxacin-susceptible microorganisms.

Considerations should be given to official guidance on the appropriate use of antibacterial agents. Oftaquix Unit Dose 5 mg/ml eye drops are indicated in adults, children aged ≥1 year to 12 years and adolescents aged 12 to 18 years.

This application was submitted under Article 8.3 of Directive 2001/83 (as amended), for a known active substance. The product is a line extension, with a change or addition of a new pharmaceutical form. The original product is the preserved product Oftaquix 5 mg/ml eye drops (PL 16058/0006), which was approved in the UK on 31 July 2001.

Levofloxacin is the S-(-) optical isomer of ofloxacin and is a broad spectrum anti-infective compound, with similar physicochemical, pharmacological and toxicological properties compared to other marketed fluoroquinolones. It has been demonstrated in *in vivo* and *in vitro* studies to be up to four times more active than ofloxacin.

No new non-clinical studies were conducted, which is acceptable given that the application was based on a well-known active substance that has been used in other previously granted licences.

Clinical studies concerning pharmacokinetic properties on Oftaquix Unit Dose 5 mg/ml Eye Drops were carried out in accordance with Good Clinical Practice (GCP). The clinical programme showed that Oftaquix Unit Dose 5 mg/ml Eye Drops provides satisfactory clinical benefits.

A Marketing Authorisation was granted in the UK on 21 June 2006.

Following a mutual recognition procedure that concluded on 30 April 2007 with the UK as Reference Member State (RMS), Denmark, Finland, Germany, Iceland, Italy and Sweden also agreed to grant a product licence for Oftaquix® Unit Dose 5 mg/ml eye drops in single-dose container (UK/H/0464/002/MR).

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture and assembly of this product prior to granting its national authorisation.

For manufacturing sites within the community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

II QUALITY ASPECTS

II.1 Introduction

One ml of eye drops, solution, contains 5.12 mg of levofloxacin hemihydrate equivalent to 5 mg of levofloxacin. Other ingredients consist of pharmaceutical excipients sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

The product is packaged in low-density polyethylene (LDPE) single-dose containers.
The single dose containers in strips of 10 are packed into paper coated, aluminium-polyethylene foil pouches to prevent water loss of the solution. There are overall pack sizes of 10, 20, 30 and 60 single-dose containers per pack.

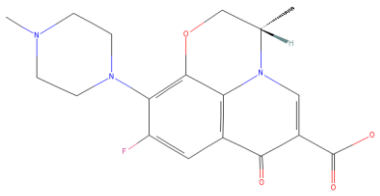
Not all pack sizes may be marketed. However, the company have committed to providing the licensing authority with the mock-ups for any pack size before marketing.

Satisfactory specifications and certificates of analysis have been provided for all packaging components.

II.2. Drug Substance

INN:	Levofloxacin hemihydrate
Chemical name:	(-)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1, 2,3-de]-[1,4]-benzoxazine-6-carboxylic acid hemihydrate

Structural formula:



Molecular formula:	$C_{18}H_{20}FN_3O_4 \cdot 1/2H_2O$
Molecular weight:	370.38
Appearance:	White to off-white, crystalline powder
Solubility	Light yellowish white to yellowish white crystals or crystalline powder.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Batch analyses data are provided that comply with the proposed specification.

Satisfactory Certificates of Analysis have been provided for all working standards used.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3. Medicinal Product

Pharmaceutical Development

The aim of the development programme was to produce an eye drop solution containing levofloxacin 5 mg/ml, but without the preservative benzalkonium chloride.

The product is a simple aqueous solution with pH adjustment. The formulation is entirely based on the multi-dose product except for the presence of preservative which is removed, with the difference in quantity being made up with water for injections.
Consequently there is no formulation development.

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature and have been optimised on the basis of results from development studies.

Manufacturing Process

Satisfactory batch formulae have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated on three production-scale batches with satisfactory results.

Finished Product Specification

The finished product specification proposed is acceptable. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Stability of the Product

Stability studies were performed on three batches of the finished product and in the packaging proposed for marketing, in accordance with current guidelines. All results from stability studies were within specified limits. This data supports a shelf-life of 2 years.

The single-dose containers have to be stored in the original pouch to protect from light.

II.4 Discussion on chemical, pharmaceutical and biological aspects

There are no objections to the approval of this product from a pharmaceutical perspective.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of levofloxacin are well-known, no further non-clinical studies are required and none have been provided.

The applicant’s non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2 Pharmacology
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.3 Pharmacokinetics
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.4 Toxicology
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)
As the product is intended for generic substitution with a product that is already marketed, no increase in environmental burden is anticipated. Thus, non-submission of an Environmental Risk Assessment is accepted.

III.6 Discussion on the non-clinical aspects
There are no objections to the approval of this application from a non-clinical perspective.

IV CLINICAL ASPECTS
IV.1 Introduction
Levofloxacin is the S-(-) optical isomer of ofloxacin and is a broad spectrum anti-infective compound, with similar physicochemical, pharmacological and toxicological properties compared to other marketed fluoroquinolones. It has been demonstrated in *in vivo* and *in vitro* studies to be up to four times more active than ofloxacin.

Santen Oy has developed this non-preserved formulation of levofloxacin Oftaquix 5 mg/ml Eye Drops in unit-dose containers in addition to the original preserved formulation.

The main rationale for this is because there are several facts which support the using preservative-free solution, mainly:
1. Topical antibiotics containing benzalkonium chloride may delay the healing process in compromised eyes with epithelial defects.
2. Although benzalkonium chloride is known to be a weak allergen, allergic patients do exist.
3. Preservative-free unit dose formulation is more convenient and hygienic. It may enhance patient compliance.

IV.2 Pharmacokinetics
No dissolution, bioavailability, or bioequivalence studies have been performed. The applicant states in the dossier that it is assumed that similar concentrations of levofloxacin is achieved on the ocular surface by using 5 mg/ml Oftaquix multidose and unit-dose formulation based on pharmacokinetic studies.

Supportive Pharmacokinetics
As supportive evidence, the company included pharmacokinetic studies performed with preserved Oftaquix 5 mg/ml Eye Drops and unpreserved formulation in this application dossier.

In Summary:
Two pharmacokinetic studies were submitted which measured the concentrations of levofloxacin achieved in the aqueous humor after application prior to cataract surgery of either preserved (Oftaquix 5 mg/ml Eye Drops) conducted by Koch *et al* (J. Cataract Refract Surg 2005;31:1377-85) or unpreserved (Cravit ophthalmic solution, marketed by Santen in Japan) conducted by Yamada *et al* (Current Eye Research; 24:403-6).

Results
The concentration of levofloxacin in the aqueous humor was similar with both the preserved and non-preserved formulations.

In addition, three studies, 03-005, 03-006, measuring concentrations of levofloxacin eye drops with preservative in plasma and tears respectively and 95034, without preservative in plasma in 95034 were described in the dossier.

The two studies (03-005 and 03-006) using the preserved formulation demonstrated low measurable levels of levofloxacin in serum and levels above MIC_{90} in the tear fluid for at least 6 hours, respectively. In the third study, 95034, using the unpreserved formulation, levofloxacin was not detected in the serum. This latter result was at variance to study 03-005, but this was explained by the fact that the analytical technique used in this study had a level of detection of 10 ng/mL, a value that exceeded the actual levels found in study 03-005.

The indication for Oftaquix Unit Dose 5 mg/ml is for the topical treatment of extra-ocular infections. The product is an aqueous topical ophthalmic solution containing the same active substance, levofloxacin in the same concentration as the original cross-referral product, (PL 16058/0006) Oftaquix 5 mg/ml Eye Drops with preservative. The concentration of levofloxacin achieved on the ocular surface is unlikely to be affected by the absence of the relatively small amount of benzalkonium chloride preservative.

The pharmacology of levofloxacin eye drops has been adequately demonstrated in the previous MRP application MRP UK/H/464/001. Therefore, the pharmacokinetic studies submitted in the dossier and described above are superfluous to requirements in this application and are not directly relevant.

IV.3 Pharmacodynamics
No new pharmacodynamic data were submitted and none were required for an application of this type.

IV.4 Clinical efficacy
The preservation of levofloxacin's anti-infective activity may be affected by the lack of preservative in the eye drops solution filled in multi-dose container especially once the dropper bottle is opened. The packaging of the unpreserved solution in single-dose containers is required to bypass this occurrence and this has been done.

It is also noted that, since benzalkonium chloride is a preservative, it may theoretically contribute to the antimicrobial efficacy of levofloxacin in Oftaquix 5 mg/ml Eye Drops. To address this, the marketing authorisation holder has also provided *in vitro* efficacy data for the non-preserved formulation of Oftaquix Unit Dose 5 mg/ml Eye Drops, in which levofloxacin and benzalkonium chloride are tested alone as well as in combination against clinical isolates of three bacterial species known to cause bacterial conjunctivitis. The three species used were *Haemophilus influenzae, Staphylococcus aureus*, and *Streptococcus pneumoniae*. Each substance was evaluated alone as well as in combination at a ratio of 100:1 (as found in the preserved formulation). Based on MIC_{50} and MIC_{90} values measured, levofloxacin combined with benzalkonium chloride was no more or less active than levofloxacin alone for the three bacterial species tested. Based on these data, it can be concluded that the antimicrobial activity of the preservative and non-preservative formulations of the finished product are the same.

The efficacy of the (preserved) Oftaquix 5 mg/ml Eye Drops has already been established in the UK.

Non-preserved formulations
The applicant submits the two pharmacokinetic studies by Yamada *et al*, and Koch *et al*, discussed in Section Clinical Pharmacology (above), and the *in vitro* efficacy data of levofloxacin and benzalkonium chloride (tested alone as well as in combination).

In the Yamada *et al* and Koch *et al* studies, the applicant suggests that both the non-preserved unit dose formulation and preserved multi-dose Oftaquix formulation achieve similar concentrations of levofloxacin on the ocular surface as well as the aqueous humor. Therefore, this suggests that the Oftaquix (unit dose) non-preserved formulations are at least as effective as Oftaquix multidose preserved formulation in treating bacterial external ocular infections in patients ≥1 year of age caused by levofloxacin susceptible organisms.

In the *in vitro* efficacy data (also discussed above), it was shown that levofloxacin combined with benzalkonium chloride was no more or less active than levofloxacin alone for treating *Haemophilus influenzae, Staphylococcus aureus,* and *Streptococcus pneumoniae* (all known to cause bacterial conjunctivitis). Based on these data, it can be concluded that the antimicrobial activity of the preservative and non-preservative formulations of the finished product are the same.

In addition, the applicant submits that the packaging of the eye drops in unit doses is more convenient and is likely to result in better compliance.

The efficacy of the preserved formulation has already been established in a previous application. The additional data from Yamada and Koch studies show that both the preservative and non-preservative formulations achieve similar concentrations on the ocular surface and the aqueous humor. The additional in vitro data show that the lack of benzalkonium chloride does not diminish the antimicrobial activity of finished product in treating bacterial conjunctivitis.

IV.5 Clinical safety

Absence of benzalkonium chloride

The original formulation of Oftaquix 5 mg/ml Eye Drops contained 0.005% of benzalkonium chloride as a preservative. This low concentration is regarded as safe. Benzalkonium chloride is a surfactant used as a preservative in many eye drops. It is preferred by many manufacturers because of its stability, excellent antimicrobial properties and long shelf-life. However, it also exhibits toxic effects on both the tear film and corneal epithelium. It has been shown that repeated use of preserved medications negatively affects the ocular surface, especially in patients whose ocular surface is compromised (Baudouin 1996). The usual dosage duration of the treatment with Oftaquix Eye Drops is 5 days.

Adverse Effects

About 17 million patients have used preserved Oftaquix or Quixin or Cravit in the USA and Japan, respectively) during the period from August 1, 2001 to January 31, 2004. It has been generally well tolerated. Eleven serious adverse effects were reported in this time period. None of theses led to a change in the reference safety information.

Several allergic reactions have been reported and the reference safety information has been changed accordingly.

Since Oftaquix Unit Dose formulation does not contain benzalkonium chloride, its absence may increase the safety of this formulation compared to Oftaquix multidose with preservative.

Assessor's Comments on Safety

The safety of Oftaquix Eye drops with the preservative benzalkonium chloride has been previously demonstrated in the MRP application MRP UK/H/0464/001.

Non-preserved formulations

Adverse reactions.

Non-preserved levofloxacin would appear not to be any less safe than preserved, especially when administered in single unit doses because one less chemical in the formulation should be conducive to a

lower occurrence of adverse effects. In addition, allergic reactions have been reported with benzalkonium chloride and its removal can only predispose to a reduction in these.

Anti-infective properties.
In vitro data supplied have shown that benzalkonium chloride has no additional effect against *Haemophilus influenzae, Staphylococcus aureus,* and *Streptococcus pneumoniae,* which are three commonly occurring ocular pathogens. Thus, the antibacterial activity of the non-preserved and preserved formulations, and their benefits, can be considered the same.

PSUR
A Periodic Safety Update Report for Oftaquix (levofloxacin hemihydrate) Eye Drops for the period from August 1, 2001 to January 31, 2004 is included in the submission dossier. This is the period from granting of the first marketing authorisation by the UK MCA on 31 July 2001.

Approximately 10 % of patients can be expected to experience adverse reactions after topical treatment with Oftaquix. These reactions are usually mild to moderate, transient and generally restricted to the eye. The most frequently reported adverse reactions are ocular burning, decreased vision and mucous strand.

As with other fluoroquinones, allergic reactions may occur in less that 1 % of patients. Several allergic reactions have been reported during levofloxacin treatment.

The calculations of patient exposure are based on the sales data. A total of 199,000 units of Oftaquix were sold during the review period. The average patient exposure is estimated to be 5 days per bottle, the most commonly prescribed duration of treatment. An estimate of the patient exposure is therefore 199,000 patients.

During the review period a total of 661,000 units of Oftaquix (Quixin in USA) were sold with the same duration of therapy therefore the corresponding number of patients.
In Japan, 47 million units of Cravit (unpreserved Oftaquix solution in multi-dose container) were sold and the average treatment duration was 20.4 days using 2.9 bottles per patient, therefore the estimated patient exposure is approximately 16.2 million. In total, about 17 million patients have used Oftaquix (Quixin, USA and Cravit, Japan) during the review period.

The PSUR reviews a number of spontaneous reports mostly from physicians directly. In general Oftaquix 5 mg/ml Eye Drops has been well tolerated. Eleven serious adverse drug reactions were reported. It is known that 10 of these recovered and the outcome of the eleventh is unknown. None of them led to a change in the reference safety information. Several allergic reactions have been reported and the reference safety information has been changed accordingly.

For a summary of the Overall Clinical Safety, see above.

IV.6 Risk Management Plan (RMP)
The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

An acceptable Risk Management Plan for the product has been submitted.

Appropriate pharmacovigilance and risk minimisation activities have been addressed.

IV.7 Discussion on the clinical aspects

There are no objections to the approval of this product from a clinical perspective**.**

The grant of a Marketing Authorisation is recommended for this application.

V USER CONSULTATION

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY

The important quality characteristics of unpreserved Oftaquix Unit Dose 5 mg/ml Eye Drops are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

The applicant has already shown through the *in vitro* and pharmacokinetic studies performed that unpreserved Oftaquix Unit Dose 5 mg/ml Eye Drops has the same antibacterial activity as the preserved Oftaquix 5 mg/ml Eye Drops, which has already been granted a UK licence.

No new or unexpected safety concerns arise from this application.

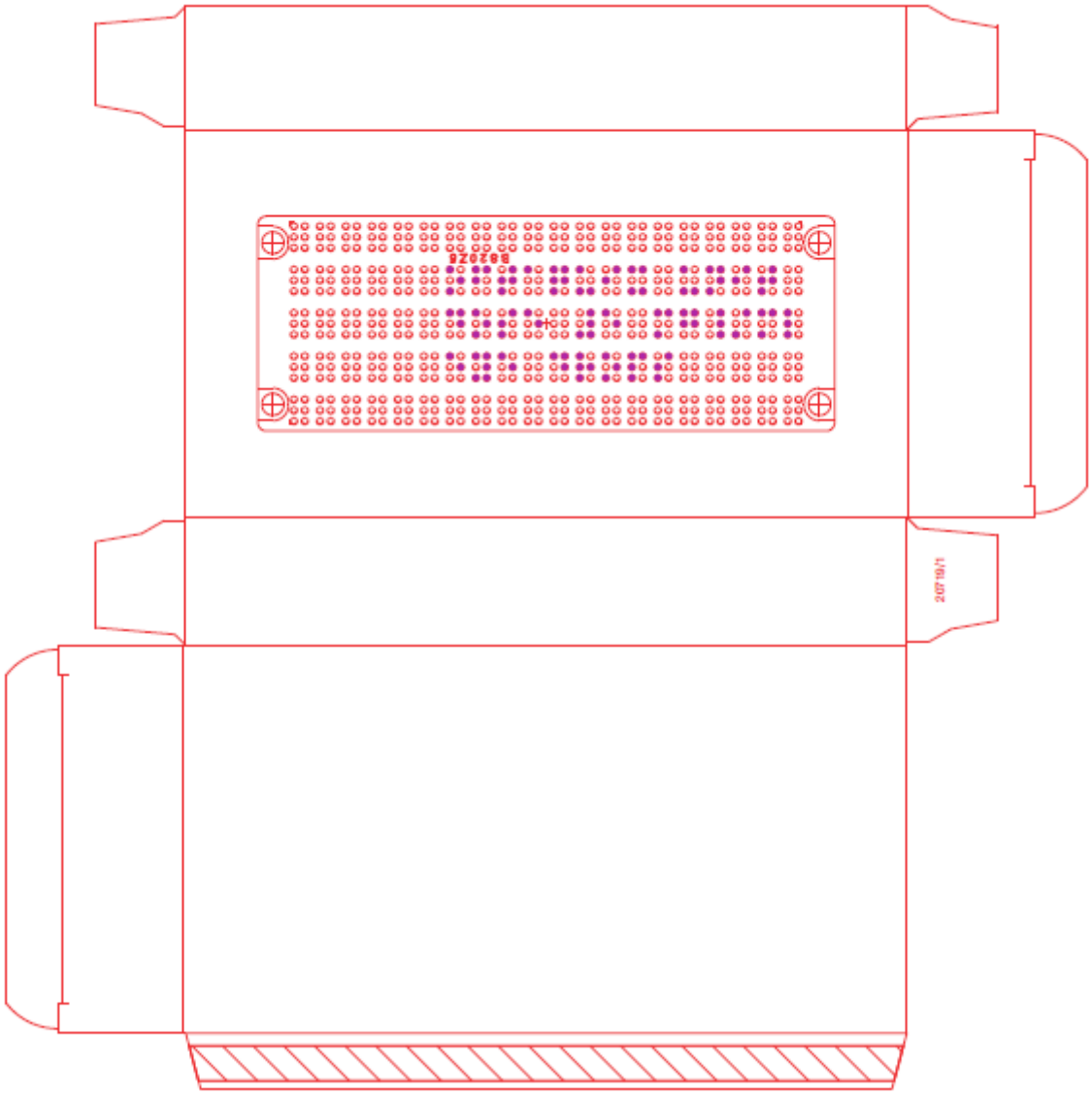
BENEFIT/RISK ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with levofloxacin is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

SUMMARY OF PRODUCT CHARACTERISTICS (SMPC), PATIENT INFORMATION LEAFLET (PIL) AND LABELS

In accordance with Directive 2010/84/EU the Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) for the product granted Marketing Authorisation at a national level are available on the MHRA website.


0.3 ml x 10
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
6 419716 601274
0.3 ml x 10
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
Eye drops, solution
in single dose container
Read the package leaflet before use.
Santen
EXP
Lot
1 ml contains 5.12 mg of levofloxacin hemihydrate equivalent to 5 mg of levofloxacin.
Sodium chloride, diluted sodium hydroxide solution or diluted hydrochloric acid and water for injections.
Ocular use.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.
POM
2071911
0.3 ml x 10
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
Santen
0.3 ml x 10
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
Santen
After first opening the pouch, the single-dose containers can be used for 3 months.
Discard any unused single-dose container after that time.
After first use: Discard any unused contents of the opened single-dose container immediately.
Store in the original pouch in order to protect from light.
PL 16058/0007
Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland
Distributor in UK:
Kestrel Ophthalmics Ltd
7 Moor Road
Broadstone
Dorset
BH18 8AZ
Licensed by:
Daiichi Sankyo Co., Ltd.
Tokyo, Japan




0.3 ml x 20
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
6 419716 601281
0.3 ml x 20
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
Eye drops, solution
in single dose container
Read the package leaflet before use.
Santen
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20800/1
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OFTAQUIX® Unit Dose
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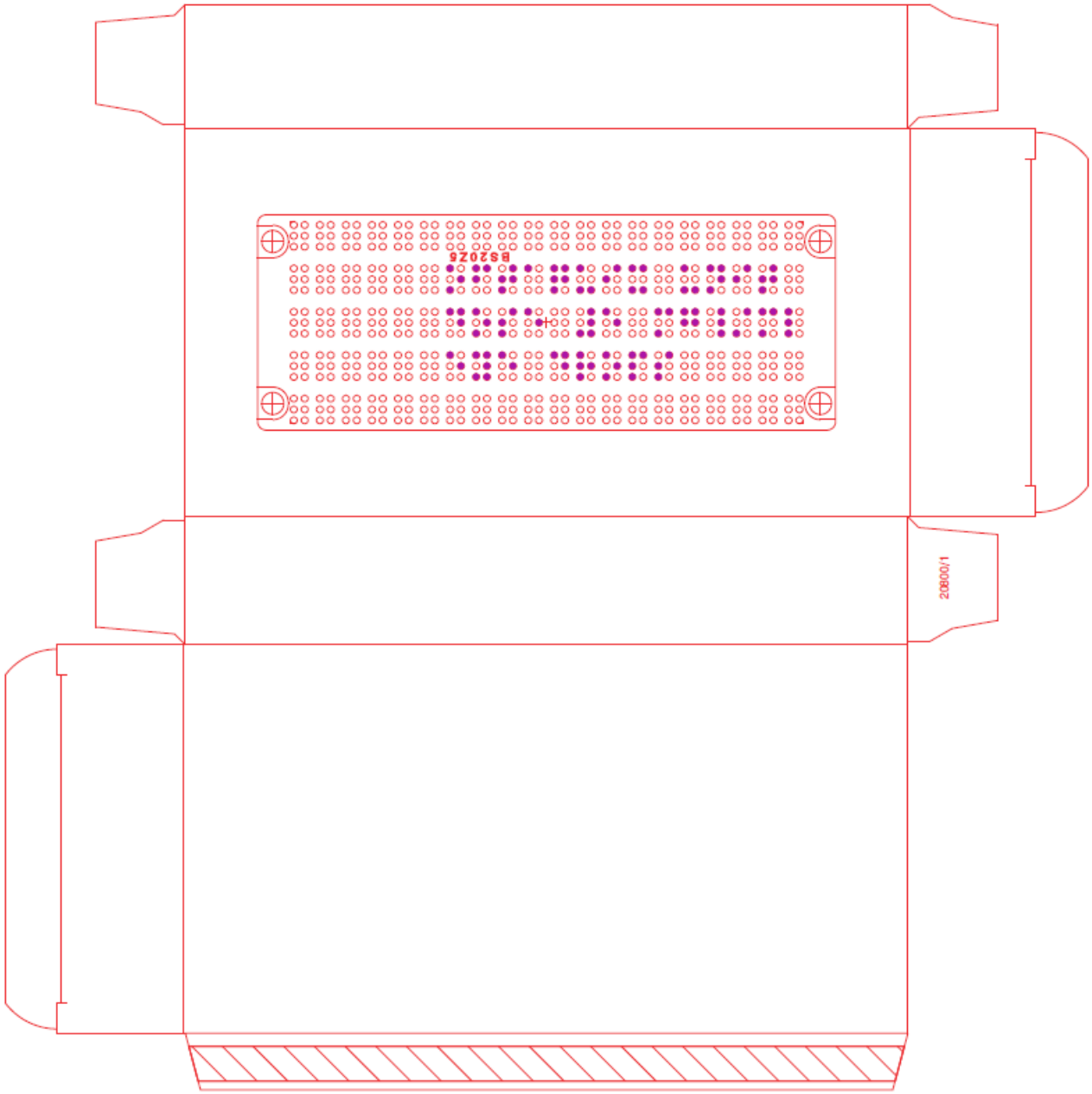
Levofloxacin
Santen
Santen Oy
Niittyhaankuja 20
33720 Tampere
Finland
Distributor in UK:
Kestrel Ophthalmics Ltd
7 Moor Road
Broadstone
Dorset
BH18 8AZ
Licenced by:
Daiichi Sankyo Co., Ltd.
Tokyo, Japan
PL 16058/0007
Store in the original pouch in order to protect from light.
After first use: Discard any unused contents of the opened single-dose container immediately.
Discard any unused single-dose container after that time.
After first opening the pouch, the single-dose containers can be used for 3 months.
Levofloxacin
5 mg/ml Eye Drops
OFTAQUIX® Unit Dose
0.3 ml x 20


BS20Z6
20800/1


0.3 ml x 30
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
6 419716 601298
0.3 ml x 30
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
Eye drops, solution
in single dose container
Read the package leaflet before use.
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Finland
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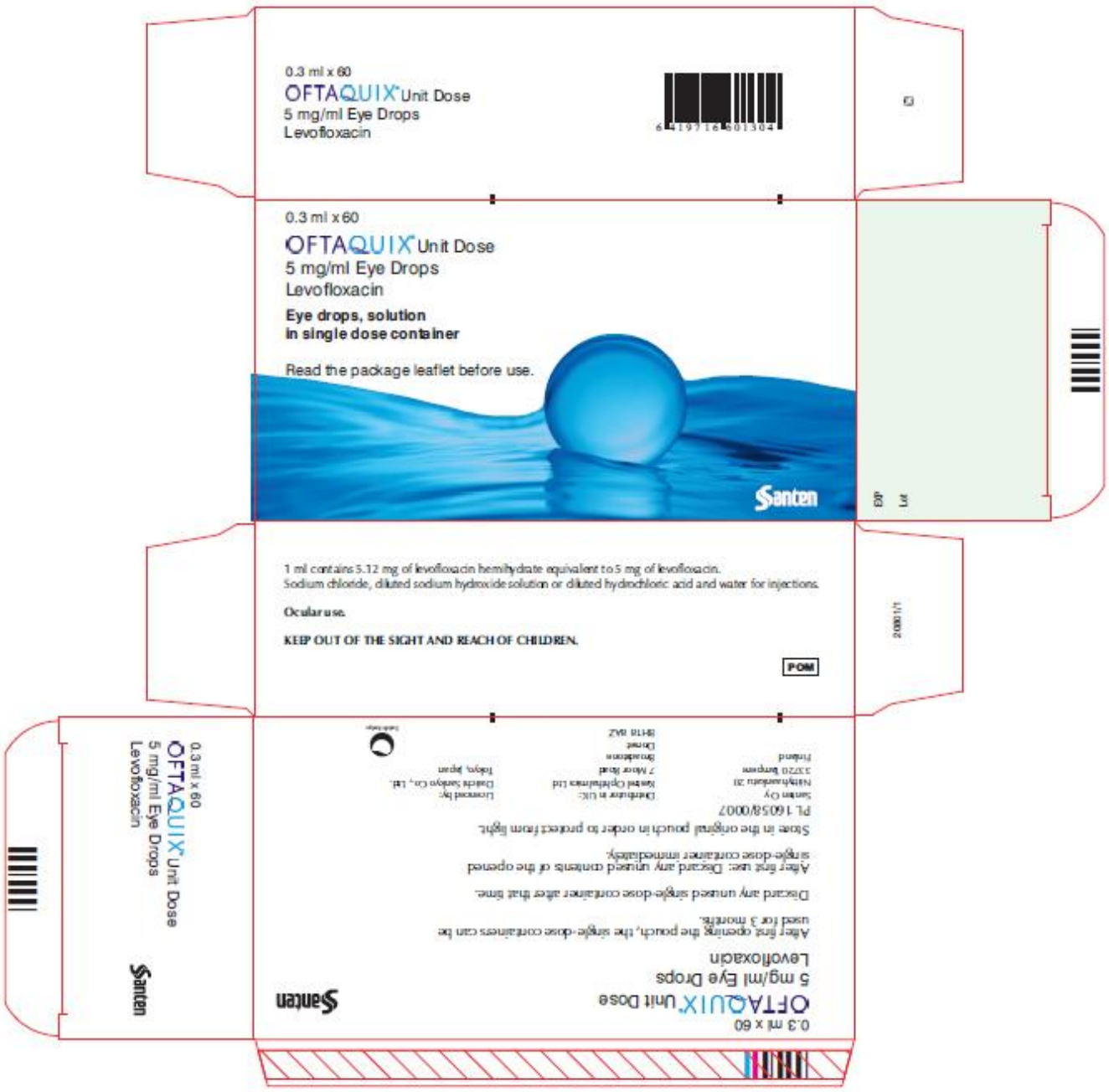
After first opening the pouch, the single-dose containers can be used for 3 months.
0.3 ml x 30
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
Santen


0.3 ml x 60
OFTAQUIX® Unit Dose
5 mg/ml Eye Drops
Levofloxacin
EXP
Lot
Eye drops, solution
in single dose container
Read the package leaflet before use.
Santen
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Ocular use.
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2008/1/1
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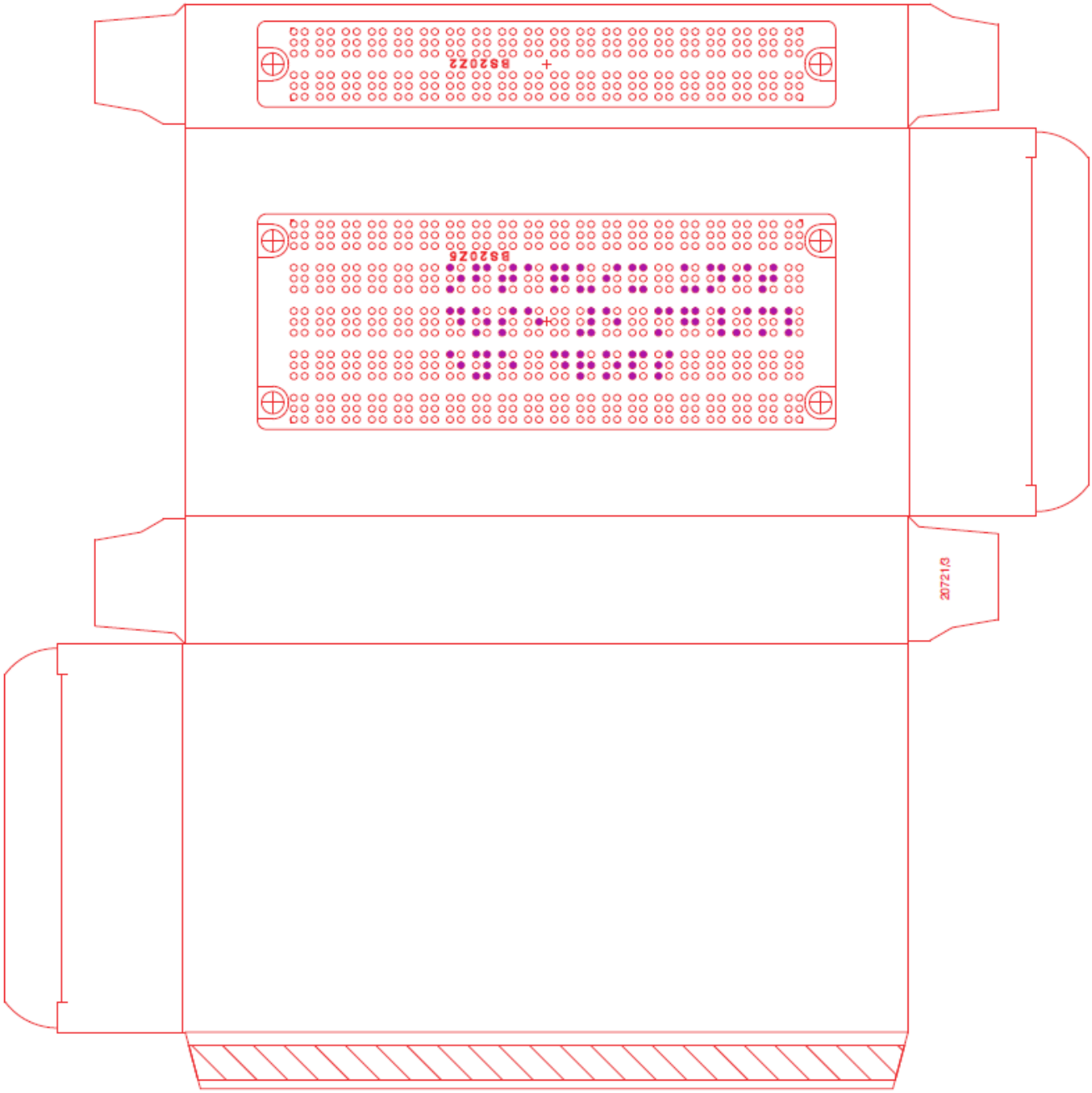
Dorset
BH18 8AZ
Licensed by:
Daiichi Sankyo Co., Ltd.
Tokyo, Japan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Levofloxacin
Eye Drops
5 mg/ml EXP:09/2016
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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

The following table lists non-urgent safety updates to the Marketing Authorisations for this product that have been approved by the MHRA since the product was first licensed. The table includes updates that have been added as an annex to this PAR. This is not a complete list of the post authorisation changes that have been made to this Marketing Authorisation.

Date submitted	Application type	Scope	Outcome
19/05/2017	Type IB	**PL 16058/0007 – 0040** To update sections 1, 2, 3, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.3 of the SmPC in line with the current QRD template, standard terms and the Excipients Guideline (NtA volume 3B)	Approved on 03/08/2017-see Annex I.

ANNEX I

Our Reference:	PL 16058/0007 - 0040
Product:	Oftaquix® Unit Dose 5 mg/ml eye drops in single dose container
Marketing Authorisation Holder:	Santen Oy
Active Ingredient(s):	Levofloxacin
Type of Procedure:	Mutual Recognition
Submission Type:	Variation
Submission Category:	Type IB
Submission Complexity:	Standard
EU Procedure Number (if applicable):	Not applicable

Reason:
To update sections 1, 2, 3, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.3 of the SmPC in line with the current QRD template, standard terms and the Excipients Guideline (NtA volume 3B).

Consequentially, the label and leaflet have been updated.

Supporting Evidence
Revised SmPC fragments, label and PIL.

Evaluation
The proposed changes to the SmPC are in line with the Quality Review Document (QRD). The updated SmPC fragments, labels and PIL have been incorporated into the Marketing Authorisation.

Conclusion
The proposed changes to the SmPC, labels and PIL are acceptable.

In accordance with Directive 2010/84/EU, the current approved UK version of the SmPC and package leaflet for this product is available on the MHRA website.

Decision - Approved on 03 August 2017.