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2023000341

National Health Care Institute
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Medicinal Products

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Our reference
2023000341

Date 25 January 2023
Subject GVS advice dexamethasone/levofloxacin (Ducressa®) eye drops

Dear Mr Kuipers,

In your letter of 3 May 2022 (CIBG-22-03786), you asked the National Health Care Institute to assess whether the medicinal product dexamethasone/levofloxacin (Ducressa®) is interchangeable with another product that is included in the Medicine Reimbursement System (GVS). The National Health Care Institute, advised by the Scientific Advisory Board (WAR), has now completed this assessment. The considerations are included in the pharmacotherapeutic report attached to this letter.

Dexamethasone/levofloxacin is indicated for prevention and treatment of inflammation, and prevention of infection associated with cataract surgery in adults. The recommended dosage is one drop every 6 hours with a treatment duration of 7 days.

The marketing authorisation holder is asking for dexamethasone/levofloxacin to be included in List 1B of the Health Insurance Regulation.

Outcome of the substantive assessment
The prevention and treatment of inflammation in general (the first part of the recorded indication) has not been investigated, so this assessment focuses on the prevention of infections after cataract surgery.

Dexamethasone/levofloxacin is an eye drop with a combination of a corticosteroid and an antibiotic. The treatment with dexamethasone/levofloxacin in the prevention of infections after cataract surgery has been studied in a randomised, non-blinded study and compared to dexamethasone/tobramycin (Tobradex®) eye drops. The results of this study show that dexamethasone/levofloxacin and dexamethasone/tobramycin do not differ based on the number of patients without signs of inflammation of the anterior eye chamber and based on adverse effects. Endophthalmitis (a serious inflammation of the eye) did not appear in either treatment arms. Based on this study, it can be concluded that dexamethasone/levofloxacin is non-inferior to dexamethasone/tobramycin. This means that the medicinal product is not less effective and therefore at least has an equal effectiveness as dexamethasone/tobramycin on the above-mentioned

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outcome parameters. Whether dexamethasone/levofloxacin has a clinically relevant effect on the other crucial outcome parameters toxic anterior segment syndrome and cystoid macula oedema (CMO), has not been investigated.

Although dexamethasone/levofloxacin eye drops have been prescribed for some time after cataract surgery to prevent infections, a combination eye drop of a corticosteroid and an antibiotic after cataract surgery is no longer included in the Dutch cataract guideline revised in 2021. The guideline now advises that at the end of a cataract operation, intracameral cefuroxime should be administered and that after the operation only preventive corticosteroid eye drops should be administered. Antibiotic drops, separately or in combination with a corticosteroid, are not included in the guideline. European data also suggest that post-operative antibiotic drops do not offer any additional benefits in addition to intracameral cefuroxime to reduce the risk of postoperative endophthalmitis. Dexamethasone/levofloxacin has not been studied in addition to intracameral cefuroxime and/or in relation to corticosteroid eye drops.

The available data show that dexamethasone/levofloxacin and dexamethasone/tobramycin do not differ on the indicated outcome parameters. This is sufficient for market registration. But for a number of crucial outcome parameters, essential data are missing. In addition, for both dexamethasone/levofloxacin and dexamethasone/tobramycin, no studies are available in which a comparison is made with corticosteroid eye drops monotherapy. The National Health Care Institute has therefore concluded, advised by its Scientific Advisory Board, that dexamethasone/levofloxacin does *not* meet the established medical science and medical practice for this indication.

Context of the assessment
According to the GIP database, in 2021 144,760 insured persons used dexamethasone/tobramycin eye drops. About half of the prescriptions were prescribed to patients who also had cataract surgery in that year. It is unclear for which indications dexamethasone/tobramycin eye drops are also prescribed. The current assessment of dexamethasone/levofloxacin only relates to the indication 'the prevention of infections after cataract surgery'. This shows that both dexamethasone/levofloxacin and dexamethasone/tobramycin do not meet the established medical science and medical practice for this indication. It has not been assessed whether dexamethasone/tobramycin meets the established medical science and medical practice for indications other than after cataract surgery.

The frequent prescription of a medicinal product, while this does not comply with the current Dutch guideline, is not commonplace during the assessments of the National Health Care Institute. It was therefore decided to invite the occupational group, the Dutch Society of Ophthalmology (NOG), to discuss the placement of these eye drops. This consultation has since taken place. It emerged that the occupational group does indeed no longer see a place for eye drops with a combination of a corticosteroid and an antibiotic after cataract surgery. The interim consultation with the occupational group has led to a longer duration of the assessment.

Advice on inclusion in the GVS
Given that no added value has been demonstrated for the use of eye drops with a

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combination of a corticosteroid and an antibiotic after cataract surgery, and that these combination eye drops no longer have any place in the Dutch guideline, the National Health Care Institute recommends that dexamethasone/levofloxacin (Ducressa®) should not be included in the GVS. In addition, the National Health Care Institute recommends that dexamethasone/tobramycin (Tobradex®))no longer be designated as an insurable performance for the indication 'to prevent infections after cataract surgery' and no longer be included in the GVS for that indication. The National Health Care Institute therefore recommends that the following reimbursement conditions apply:
Dexamethasone/tobramycin condition
Only for an insured person who is prescribed this medicinal product for a treatment other than after cataract surgery.

To allow the occupational group time to adjust their prescribing behaviour, we would suggest that you observe a transitional period and include the condition in List 2 from June 2023.

Yours sincerely,

Sjaak Wijma,
Chairperson of the Executive Board