HAUTE AUTORITÉ DE SANTÉ

# TRANSPARENCY COMMITTEE
## SUMMARY
## 7 JULY 2021

*The legally binding text is the original French opinion version*

***dexamethasone***
**OZURDEX 700 micrograms intravitreal implant in applicator**

**Re-evaluation**

### Key points

Favourable opinion for reimbursement only in the treatment of visual impairment due to diabetic macular oedema (DME) in adults with a visual acuity of less than or equal to 5/10 and in whom diabetes management has been optimised, in patients who are:

- pseudophakic,
- considered insufficiently responsive to non-corticosteroid therapy,
- or considered unsuitable for non-corticosteroid therapy.

Unfavourable opinion for reimbursement in other situations.

### What therapeutic improvement?

No clinical added value in the therapeutic strategy.

## Role in the care pathway?

Optimisation of diabetes management and its risk factors (glucose, blood pressure and lipid balance and quitting smoking) is a prerequisite to any treatment for visual impairment due to diabetic macular oedema (DME). Control of blood glucose and blood pressure, within the limits required by learned societies, can make it possible to control progression of the retinopathy or DME.

Among the other types of management available, focal laser photocoagulation, which is the standard treatment, is reserved for focal forms of macular oedema located away from the fovea, and possibly cases of severe DME involving the central region, where there are leaks from micro-aneurysms accessible via laser treatment and when visual acuity is normal. This technique does not improve visual acuity.
Medicinal treatments include anti-VEGF intravitreal injections (ranibizumab and aflibercept) and corticosteroid intravitreal implants [OZURDEX (dexamethasone) and ILUVIEN, (fluocinolone acetonide)].
Anti-VEGF [ranibizumab (LUCENTIS) and aflibercept (EYLEA)] intravitreal injections are first-line treatments when the visual impairment is associated with a diffuse form of DME or leakages close to the centre of the macula.
The MA for OZURDEX (dexamethasone) limits its use, firstly, to patients who are pseudophakic or who are unsuitable for non-corticosteroid therapy - subpopulations in which it is considered to be a first-line treatment - and, secondly, to patients insufficiently responsive to non-corticosteroid therapy, i.e. as second-line treatment.
For anti-VEGF therapies, as for OZURDEX (dexamethasone), the Committee recommends that these treatments be used when visual acuity has decreased to less than or equal to 5/10 and diabetes management has been optimised.
The choice between anti-VEGF therapies [ranibizumab (LUCENTIS) and aflibercept (EYLEA)] and OZURDEX (dexamethasone) in pseudophakic patients is left to the decision of the ophthalmologist, who should take into account the ophthalmological characteristics of the treated eye, the diabetic retinopathy stage, as well as the patient's cardiovascular and cerebrovascular history and capacities to comply with treatment.

In chronic DME, a fluocinolone acetonide intravitreal implant (ILUVIEN) is a therapeutic option, in the event of failure of other treatments, particularly anti-VEGF therapies, OZURDEX (dexamethasone) and laser therapy, if management of diabetes is optimised, taking into account its safety profile (risk of glaucoma, cataract).

DME associated with vitreomacular traction is the only clinical form for which surgery remains the treatment of choice. This form of DME is rare: it is estimated to concern less than 5% of oedemas.

**Role of OZURDEX (dexamethasone) in the care pathway**

OZURDEX (dexamethasone) has a role in the treatment of visual impairment due to diabetic macular oedema when visual acuity is less than or equal to 5/10 and diabetes management has been optimised, in the following situations:

- **as first-line treatment** in patients who are pseudophakic or who are considered unsuitable for non-corticosteroid therapy,

- **as second-line treatment** in patients who are considered insufficiently responsive to non-corticosteroid therapy.

The choice between anti-VEGF therapies [ranibizumab (LUCENTIS) and aflibercept (EYLEA)] and OZURDEX (dexamethasone intravitreal implant) in the first-line treatment of pseudophakic patients is left to the decision of the ophthalmologist, who should take into account the ophthalmological characteristics of the treated eye [history of glaucoma or ocular hypertonia, lens status (phakic or pseudophakic), history of vitrectomy], the diabetic retinopathy stage, as well as the patient's cardiovascular and cerebrovascular history, age and capacities to comply with treatment.

## COMMITTEE'S CONCLUSIONS

**Considering all of this information and further to debate and voting, the Committee considers:**

## Clinical benefit

◗ Diabetic macular oedema (DME) is a complication of diabetic retinopathy. It is asymptomatic but progresses gradually to visual impairment and blindness, resulting in disability and a marked deterioration in quality of life.

◗ The proprietary medicinal product OZURDEX (dexamethasone) intravitreal implant is a curative medicine for visual impairment due to DME in patients who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy.

◗ Its efficacy/adverse effects ratio remains low.

◗ There are therapeutic alternatives to this medicinal product.

◗ OZURDEX (dexamethasone) has a role in the treatment of visual impairment due to diabetic macular oedema when visual acuity is less than or equal to 5/10 and diabetes management has been optimised, in the following situations:
- **as first-line treatment** in patients who are pseudophakic or who are considered unsuitable for non-corticosteroid therapy,
- **as second-line treatment** in patients who are considered insufficiently responsive to non-corticosteroid therapy.

◗ **Public health impact**

Considering:
- the seriousness of DME, which causes visual impairment and is the leading cause of blindness in patients under the age of 50;
- the prevalence of DME in diabetics, estimated to be 3%;
- the partially met medical need in the treatment of visual impairment due to DME in patients who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy;
- the lack of response to the identified partially met need in view of:
    - the low improvement in best corrected visual acuity observed with OZURDEX (dexamethasone) in clinical studies and in the LOUVRE 3 post-registration study (below the clinical relevance threshold of 5 letters);
    - the absence of specific data in the patient subgroups defined by the MA (patients who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy);
    - the absence of comparison with anti-VEGF therapies;
    - the specific adverse reaction risks associated with the administration of an intraocular corticosteroid and observed with OZURDEX (dexamethasone), such as increased intraocular pressure, cataract and conjunctival haemorrhage;
    - the lack of a demonstrated impact on quality of life, a particularly important aspect in this disabling disease;

- the absence of demonstration of an additional impact on the organisation of care and the care and life pathway of patients, despite the potential benefit of having access with OZURDEX (dexamethasone) to a treatment making it possible to reduce the number of injections compared to anti-VEGF therapies, and considering:
  - the persistence of doubts with respect to the 6-monthly administration frequency, which does not appear to be optimal (loss of efficacy from the fourth month, on average, following injection);
  - the need for regular patient monitoring due to the specific adverse reactions associated with the administration of an intraocular corticosteroid;

OZURDEX (dexamethasone) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of OZURDEX (dexamethasone) 700 micrograms intravitreal implant in applicator remains <u>moderate</u> in the treatment of visual impairment due to diabetic macular oedema (DME) in adults with a visual acuity of less than or equal to 5/10 and in whom diabetes management has been optimised, in patients who are:**
- **pseudophakic,**
- **considered insufficiently responsive to non-corticosteroid therapy,**
- **or considered unsuitable for non-corticosteroid therapy.**

**It remains <u>insufficient</u> in the other situations.**

**The Committee issues a favourable opinion for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in "the treatment of visual impairment due to diabetic macular oedema (DME) in adults with a visual acuity of less than or equal to 5/10 and in whom diabetes management has been optimised, in patients who are:**
- **pseudophakic,**
- **or considered insufficiently responsive to non-corticosteroid therapy,**
- **or considered unsuitable for non-corticosteroid therapy."**

**and at the MA dosages.**

**The Committee issues an unfavourable opinion for reimbursement in other situations.**

- **Recommended reimbursement rate: 30%**

## Clinical Added Value

- **In the treatment of visual impairment due to diabetic macular oedema (DME) in adults with a visual acuity of less than or equal to 5/10 and in whom diabetes management has been optimised, in patients who are:**
  - **pseudophakic,**
  - **considered insufficiently responsive to non-corticosteroid therapy,**
  - **or considered unsuitable for non-corticosteroid therapy.**

**Considering:**

- **the low improvement in visual acuity, below the clinical relevance threshold, observed with OZURDEX (dexamethasone) in the MEAD 010 and 011 randomised, single-blind placebo-controlled studies and in the LOUVRE 3 observational study that was discontinued prematurely;**
- **the specific adverse reaction risks associated with the administration of an intraocular corticosteroid and observed with OZURDEX (dexamethasone), such as increased intraocular pressure, cataract and conjunctival haemorrhage;**
- **the absence of randomised comparative studies having compared the efficacy and safety of OZURDEX (dexamethasone) with those of anti-VEGF therapies (ranibizumab and aflibercept) in the medium and long term;**
- **the absence of a demonstrated improvement in terms of quality of life compared to anti-VEGF therapies;**

**the Committee considers that OZURDEX (dexamethasone) provides no clinical added value (CAV V) in the care pathway, including, in particular the anti-VEGF therapies LUCENTIS (ranibizumab) and EYLEA (aflibercept), for visual impairment due to DME in adults when visual acuity is less than or equal to 5/10 and diabetes management has been optimised.**