Dexamethasone intracanalicular insert (Dextenza) for pain and inflammation following cataract surgery

NIHR HSRIC ID: 8681

Lay summary

*Dexamethasone intracanalicular insert* is a new drug that is placed into the canaliculus of the eye to treat pain and inflammation in people who have had cataract surgery. A cataract is when the lens in the eye becomes cloudy causing blurred vision. Cataracts are very common and usually affect older adults. More than 300,000 cataract operations are carried out in the UK each year. The vast majority of these are successful, but complications such as inflammation do sometimes occur. Eye drops are often used to prevent pain and inflammation after cataract surgery. However, not everybody uses these as often as necessary. Dexamethasone insert automatically delivers medication for the entire course of treatment.

This briefing is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information.

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TARGET GROUP

- Post-cataract surgery inflammation and pain.

TECHNOLOGY

DESCRIPTION

Dexamethasone intracanalicular insert (Dextenza; OTX-DP) is a sustained release formulation of the corticosteroid dexamethasone that is inserted non-invasively into the canaliculus to deliver a four week tapered release of corticosteroid to the ocular surface following surgery. It also contains a visualisation aid for retention monitoring throughout the treatment period. Once the therapy is complete, the hydrogel resorbs and exits the nasolacrimal system without further intervention.

Dexamethasone insert does not currently have a Marketing Authorisation in the EU for any indication.

Dexamethasone insert is also in phase III clinical trials for allergic conjunctivitis and phase II clinical trials for dry eye disease.

INNOVATION and/or ADVANTAGES

If licensed, dexamethasone insert will offer a self-tapered, 30 day dose of steroid therapy with a single insertion that delivers treatment to the ocular surface without the need for patients to repeatedly administer eye drops.

DEVELOPER

Ocular Therapeutix, Inc.

AVAILABILITY, LAUNCH OR MARKETING

In phase III clinical trials.

PATIENT GROUP

BACKGROUND

Cataract is a common visual impairment. Cataracts describe any opacity in the crystalline lens of the eye which can affect one or both eyes with varying levels of visual impairment. It is often the result of the normal process of aging, and can be classified by the area affected (nuclear sclerotic, cortical or posterior subcapsular cataracts). Other risk factors include diabetes, eye injury, use of corticosteroid eye drops or tablets, gender (female), sunlight, dehydration/diarrhoeal crisis, nutrition and socio-economic status. Cataract may also occur secondary to hereditary factors, inflammation, metabolic or nutritional disorders and radiation. Smoking and excessive alcohol intake is also associated with an increased risk of developing age-related cataracts. Symptoms include blurred or hazy vision, ‘washed out’ look with less contrast between black and white, glare or dazzle by bright lights at night. Colours may appear more yellow or altered.
Cataract extraction accounts for a large proportion of the surgical workload of ophthalmologists, and cataract surgery is the commonest elective surgical procedure performed in the UK\textsuperscript{2}.

**CLINICAL NEED and BURDEN OF DISEASE**

In the UK about 1 in 3 people over the age of 65 have a cataract, with many cases affecting both eyes\textsuperscript{5}. If left untreated, cataracts may result in loss of vision. However, following surgery, 95\% of people will have corrected vision assuming no other eye problems are present. Complications after surgery are rare, but may include infection, bleeding, inflammation, and worsening vision\textsuperscript{6}. Around 1 in 1,000 people suffer permanent loss of vision following cataract surgery\textsuperscript{7}.

Cataract surgery is the most common operation performed in the UK, with more than 300,000 procedures carried out each year\textsuperscript{7,8}. Around 10\% of over 65 year olds have already had cataract surgery\textsuperscript{8}. Over 90\% of cataract surgery is carried out on those aged \(\geq 60\) years old, and just under 60\% is carried out on those aged \(\geq 75\) years\textsuperscript{2}.

In 2014-15, there were 213,893 admissions for cataracts, unspecified (ICD-10 H26.9) in England, resulting in 4,793 bed days and 215,211 finished consultant episodes\textsuperscript{9}.

The population likely to be eligible to receive dexamethasone insert could not be estimated from available published sources, but patients who could be non compliant with eye drop therapy would be potentially suitable for this product\textsuperscript{a}.

**PATIENT PATHWAY**

**RELEVANT GUIDANCE**

**NICE Guidance**


**NHS England Policies and Guidance**


**Other Guidance**

- NICE Clinical Knowledge Summaries. Cataracts. September 2015\textsuperscript{10}.
- The Royal College of Ophthalmologists. Cataract Surgery Guidelines. September 2010\textsuperscript{2}.

\textsuperscript{a} Company information.
CURRENT TREATMENT OPTIONS

Surgical removal is the only effective treatment for cataract\(^2\), although if the cataract does not impair daily activities, then a change of glasses and brighter reading lights may help\(^7\). After surgery, there may be pain or discomfort for a few days, and paracetamol (but not aspirin which can cause bleeding) is recommended for analgesia\(^2\). In the event of inflammation, immediate treatment with postoperative subconjunctival steroids with or without orbital floor steroids is required\(^2\). Post operatively, intensive treatment with topical steroids and cycloplegic agents should be administered\(^2\). To avoid fibrosis occluding the papillary axis due to large fibrin plaques, recombinant tissue plasminogen activator may also be used\(^2\). Often prophylactic eye drops of steroid or NSAID active agents are administered to prevent the development of ocular pain and inflammation\(^b\). Steroid eye drops are routinely used to prevent and treat ocular pain and inflammation following cataract surgery. Many patients are either unable to, don’t remember to, or incorrectly dose themselves with steroid eye drops. Under dosing can result in persistent pain and inflammation as well as poor visual outcomes. Over dosing can lead to steroid induced glaucoma development. Thus consistent dosing that can be automatically delivered is desirable. There is also no preservative free steroid eye drop available to patients. The frequent use of preserved eye drops can compromise the ocular surface, leading to the development of dry eye syndrome\(^b\).

EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02736175, OTX-15-003; dexamethasone insert vs placebo; phase III.</td>
<td>NCT02034019, OTX-13-002; dexamethasone insert vs placebo; phase III.</td>
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<tr>
<td>Sponsor</td>
<td>Ocular Therapeutix, Inc.</td>
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<td>Status</td>
<td>Ongoing.</td>
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<td>Source of information</td>
<td>Trial registry(^12), manufacturer.</td>
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<td>Location</td>
<td>USA.</td>
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<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
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<tr>
<td>Participants</td>
<td>n=436 (planned); aged ≥18 years; has cataract and expected to undergo clear corneal cataract surgery with phacoemulsification and implantation of posterior chamber lens; potential post-operative pinhole corrected Snellen visual acuity (VA) of 20/200 or better in both eyes; no intraocular inflammation in the study eye present during the screening slit lamp examination or score &gt;0 on the Ocular Pain Assessment in the study eye at screening.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Randomised to single placement of dexamethasone insert 0.4mg or placebo drug delivery vehicle.</td>
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<tr>
<td>Follow-up</td>
<td>Sustained and tapered release of dexamethasone over 30 days. Subjects undergo follow-up visits to post-operative day 45.</td>
</tr>
<tr>
<td>Primary outcome/s</td>
<td>Absence of cells (i.e. score of ‘0’) in the anterior chamber of the eye at day 14; absence of pain (i.e. score of ‘0’) in the</td>
</tr>
</tbody>
</table>

\(^b\) Company information.
### Key results

For dexamethasone vs placebo, respectively:
- Absence of ocular pain on days: 2 (71.2% vs 45.8%; p=0.0001), 4 (77.9% vs 52.4%; p=0.0001), 8 (80.4% vs 43.4%; p<0.0001), and day 14 (79.6% vs 39.8%; p<0.0001); absence of anterior chamber cells at day 14 in the study eye, 33.1% (54/164) vs. 14.5% (12/83; p=0.0018); absence of anterior chamber flare, on day 8 (52.1% vs 32.9%; p=0.0044) and day 14 (71.6% vs 36.1%; p< 0.0001); mean anterior chamber cell scores, day 8 (0.90 vs 1.30; p=0.0008) and day 14 (0.67 vs 1.17; p=0.0002).

### Adverse effects (AEs)

No serious adverse events (SAEs) related to treatment. All AEs were transient and resolved over the course of the study.

For dexamethasone vs placebo groups, respectively:
- Number of AEs, 98 vs 59; pts with at least 1 AE, 67 (41.4%) vs 39 (46.4%); number of pts with at least 1 ocular AE, 55 (34.0%) vs 36 (42.9%); number of pts with at least 1 ocular AE in study eye, 48 (29.6%) vs 34 (40.5%); serious non-ocular AE, 3 vs 4; serious ocular AE, 0 vs 1; treatment related AEs, 2 vs 1.

### Expected reporting date

Study completion date reported as Jan 2017.

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<table>
<thead>
<tr>
<th>Study eye at day 8 as assessed by NIH Numerical Rating Scale.</th>
<th>Cells in anterior chamber of the study eye; pain in the study eye; flare in their anterior chamber of the study eye.</th>
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</thead>
<tbody>
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<td>Secondary outcome/s</td>
<td>Anterior chamber cells score in the study eye; pain score in the study eye; absence of flare in the anterior chamber.</td>
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<th>NCT01666210, OTX-12-002; dexamethasone insert vs placebo; phase II.</th>
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<td>Source of information</td>
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<td>Poster&lt;sup&gt;16&lt;/sup&gt;, trial registry&lt;sup&gt;17&lt;/sup&gt;, manufacturer.</td>
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<td>Design</td>
<td>Randomised, placebo-controlled</td>
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<td>Participants</td>
<td>n=241; aged ≥18 years; has cataract and expected to undergo clear corneal cataract surgery with phacoemulsification and implantation of posterior chamber lens; potential post-operative pinhole corrected Snellen VA of 20/200 or better in both eyes; no intraocular inflammation in the study eye present during the screening slit lamp examination or score &gt;0 on the Ocular Pain Assessment in the study eye</td>
<td>n=59; aged ≥21 years; has cataract and expected to undergo clear corneal cataract surgery with phacoemulsification and implantation of posterior chamber lens; no intraocular inflammation in the study eye present during the screening slit lamp examination or score &gt;0 on the Ocular Pain Assessment in the study eye</td>
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<td><strong>Horizon Scanning Research &amp; Intelligence Centre</strong></td>
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**screening slit lamp examination or score >0 on the Ocular Pain Assessment in the study eye at screening.**

**Schedule**

| Randomised to single implantation of dexamethasone insert 0.4mg or placebo drug delivery vehicle. |

**Follow-up**

| Sustained and tapered release of dexamethasone over 30 days. Subjects undergo follow-up visits to post-operative day 60. |

**Primary outcome/s**

| Absence of cells in anterior chamber of the study eye at day 14; absence of pain in the study eye at day 8. |

**Secondary outcome/s**

| Absence of anterior chamber flares; mean anterior chamber cell score |

| AEs; flare in the anterior chamber of the study eye; presence of the drug delivery vehicle at all study visit points. |

| Key results |

For dexamethasone vs placebo, respectively:
- absence of ocular pain on days: 2 (65.6% vs 40.0%; p=0.0002), 4 (73.6% vs 48.8%; p=0.0001), 8 (77.5% vs 58.8%; p=0.0025), and day 14 (76.9% vs 57.5%; p=0.0019); absence of anterior chamber cells at day 14 in the study eye, 39.4% (63/161) versus 31.3% (25/80; p=0.2182); absence of anterior chamber flare on day 8 (63.1% vs 46.3%; p=0.0127) and day 14 (66.3% vs 48.8%; p<0.0090); mean anterior chamber cell scores, day 8 (0.72 vs 1.08; p=0.0001) and day 14 (0.55 vs 1.08; p=0.0001). |

For dexamethasone vs placebo groups, respectively on day 30:
- absence of cells in the anterior chamber, 62% vs 14%; absence of flare in the anterior chamber, 79% vs 28%; absence of pain, 79% vs 28%. |

No intraocular pressure spikes or creeps with dexamethasone observed.

| Adverse effects (AEs) |

No SAEs related to treatment. All AEs were transient and resolved over the course of the study.

For dexamethasone vs placebo groups, respectively:
- number of AEs, 74 vs 47; pts with at least 1 AE, 57 (35.6%) vs 38 (47.5%); number of pts with at least 1 ocular AE, 50 (31.3%) vs 33 (41.3%); number of pts with at least 1 ocular AE in study eye, 46 (28.8%) vs 31 (38.8%); serious non-ocular AE, 2 vs 3; serious ocular AE, 0 vs 0; treatment related AEs, 1 vs 1. |

No SAEs related to treatment. All AEs were transient and resolved over the course of the study.

**ESTIMATED COST and IMPACT**

**COST**

The cost of dexamethasone punctum plug is not yet known.
IMPACT - SPECULATIVE

Impact on Patients and Carers

- Reduced mortality/increased length of survival
- Reduced symptoms or disability
- Other: reduced need for administration of eye drops by patients or carers.
- No impact identified

Impact on Health and Social Care Services

- Increased use of existing services
- Decreased use of existing services
- Re-organisation of existing services
- Need for new services
- None identified

Impact on Costs and Other Resource Use

- Increased drug treatment costs
- Reduced drug treatment costs
- Other increase in costs:
- Other reduction in costs:
- Other: uncertain unit cost compared to current alternative treatments.
- None identified

Other Issues

- Clinical uncertainty or other research question identified:
- None identified

REFERENCES


