Voclosporin (LX-211) for non-infectious uveitis

August 2008

This technology summary 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.
Voclosporin (LX-211) for non-infectious uveitis

Target group
- Non-infectious uveitis.

Background
Uveitis is inflammation of the uveal tract which consists of the iris, the ciliary body and the choroid. Uveitis is commonly classified by the anatomical location of the pathology into: anterior, intermediate, posterior or diffuse. It may be acute or chronic and recurrent. Symptoms of uveitis can include: pain, redness, photophobia, headaches, floaters and decreased visual acuity. Non-infectious uveitis may be due to an underlying inflammatory condition, an autoimmune disorder or as a result of trauma to the eye. In many cases the cause remains uncertain.

Technology description
Voclosporin (LX-211, Luveniq) belongs to the ciclosporin class of drugs. It is a calcineurin inhibitor which suppresses the immune response by reversibly inhibiting T-cell proliferation and the release of pro-inflammatory cytokines. The intended use of voclosporin is for the treatment of active and quiescent non-infectious uveitis in addition to, or as a substitute for, current therapies. It is administered orally at 0.2, 0.4 or 0.6mg twice daily.

Voclosporin is also in phase III clinical trials for psoriasis and phase IIb trials for the prevention of renal transplant rejection.

Innovation and/or advantages
Voclosporin may have higher efficacy and fewer side-effects than currently available treatments.

Developer
Lux Biosciences Inc.

Availability, launch or marketing dates, and licensing plans:
In phase III clinical trials.

Relevant guidance

Clinical need and burden of disease
The existence of self-resolving forms of uveitis makes it difficult to ascertain its true incidence. However, the annual incidence in western countries is estimated at approximately 17 per 100,000 people (about 9100 people in England and Wales), while the prevalence of uveitis is estimated at about 38 per 100,000 people (about 20,400 people in England and Wales)^2. Anterior uveitis is the most common form of the disease accounting for 75% of cases^3. It is equally common in men and women, and more than 90% of cases occur in people older than 20 years of age^4.

Inappropriate management of uveitis can lead to significant complications and permanent loss of vision. Complications include: increased eye pressure, glaucoma, vascular occlusions and optic neuropathy, retinal detachment, neovascularisation of the retina,
optic nerve or iris, cystoid macular oedema, macular ischaemia and cataracts. It is estimated that uveitis accounts for 10% of all cases of blindness globally.

**Existing comparators and treatments**

Treatment is dependent on the type of uveitis, severity and cause. Current options include:

- **Cyclopegics (drops to dilate the pupil):**
  - Cyclopentolate
  - Atropine sulphate

- **Steroids - The prolonged use of steroids can cause steroid glaucoma and/or steroid cataract:**
  - Prednisolone eye drops
  - Rimexolone
  - Steroid injection or systemic steroid therapy (in more severe cases).

- **NSAIDs:**
  - Diclofenac eye drops (not licensed for this indication in the UK).

- **Immunosuppressive drugs (not licensed for this indication in the UK):**
  - Cyclosporine A
  - Tacrolimus
  - Azathioprine
  - Mycophenolate mofetil
  - Mycophenolic acid
  - Methotrexate

**Efficacy and safety**

<table>
<thead>
<tr>
<th>Trial name or code</th>
<th>NCT00404885*: active non-infectious anterior uveitis; LX-211 vs placebo; phase III.</th>
<th>NCT00404742*: clinically quiescent non-infectious intermediate anterior, intermediate posterior or pan-uveitis; LX-211 vs placebo; phase III.</th>
<th>NCT00404612*: active sight threatening, non-infectious intermediate-, anterior and intermediate-, posterior-, or pan-uveitis; LX-211 vs placebo; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sponsor</strong></td>
<td>Lux Biosciences Inc.</td>
<td>Lux Biosciences Inc.</td>
<td>Lux Biosciences Inc.</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Ongoing</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Worldwide</td>
<td>Worldwide</td>
<td>Worldwide</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Randomised, double-blind, placebo control.</td>
<td>Randomised, double-blind, placebo control.</td>
<td>Randomised, double-blind, placebo control.</td>
</tr>
<tr>
<td><strong>Participants in trial</strong></td>
<td>n= 100 planned; adults; uveitis; active, non-infectious, anterior. Randomised to: LX211 0.2, 0.4 or 0.6 mg/kg twice a day or placebo.</td>
<td>n= 220 planned; adults; non-infectious intermediate, anterior and intermediate, posterior or panuveitis. Randomised to: LX211 0.2, 0.4 or 0.6 mg/kg twice a day or placebo.</td>
<td>n= 210 planned; adults; non-infectious intermediate, anterior and intermediate, posterior or panuveitis. Randomised to: LX211 0.2, 0.4 or 0.6 mg/kg twice a day or placebo.</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Core protocol 24 weeks with an optional</td>
<td>Core protocol 24 weeks with an optional</td>
<td>Core protocol 24 weeks with an optional</td>
</tr>
</tbody>
</table>
**August 2008**

**National Horizon Scanning Centre**

News on emerging technologies in healthcare

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Vitreous haze.</th>
<th>extension of 24 weeks.</th>
<th>extension of 24 weeks.</th>
<th>Ocular inflammation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary outcomes</td>
<td>Corticosteroid usage; visual acuity; thickness of the macula; graded anterior chamber cells.</td>
<td>Vitreous haze; anterior chamber cells; visual acuity; corticosteroid usage.</td>
<td>Vitreous haze.</td>
<td>Ocular inflammation.</td>
</tr>
</tbody>
</table>


**Estimated cost and cost impact**

The cost of voclosporin is yet to be determined.

**Potential or intended impact – speculative**

**Patients**

- ☑ Reduced morbidity
- ☑ Quicker, earlier or more accurate diagnosis or identification of disease
- ☑ Improved quality of life for patients and/or carers
- ☑ Other:
- ☑ None identified

**Services**

- ☑ Increased use
- ☑ Decreased use
- ☑ Service reorganisation required
- ☑ Staff or training required
- ☑ Other:
- ☑ None identified

**Costs**

- ☑ Increased unit cost compared to alternative
- ☑ New costs:
- ☑ Increased costs: more patients coming for treatment
- ☑ Savings: steroid sparing, reducing complications.
- ☑ Increased costs: capital investment needed
- ☑ Other:
- ☑ None identified

**References**

The National Institute for Health Research National Horizon Scanning Centre Research Programme is funded by the Department of Health. The views expressed in this publication are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

The National Horizon Scanning Centre,
Department of Public Health and Epidemiology
University of Birmingham, Edgbaston, Birmingham, B15 2TT, England
Tel: +44 (0)121 414 7831 Fax +44 (0)121 414 2269
www.pcpoh.bham.ac.uk/publichealth/horizon