Intepirdine for dementia with Lewy bodies

NIHR HSRIC ID: 12196

Lay summary

*Intepirdine* is a new drug to treat patients with dementia with Lewy bodies. Lewy bodies are deposits of an abnormal protein inside brain cells. These deposits build up in areas of the brain responsible for things such as memory and muscle movement. It is not clear why the deposits develop and how exactly they damage the brain. Intepridine is taken by mouth and causes the release of chemicals in the brain that may improve cognition and function. There is currently no cure for dementia with Lewy bodies or any medication that slow progression down.

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

- Dementia with Lewy bodies.

TECHNOLOGY

DESCRIPTION

Intepirdine (RVT-101; SB-742457; GSK 742457) is a serotonin 6 receptor antagonist which causes the release of acetylcholine and other neurotransmitters that may improve cognition and function in dementia with Lewy bodies. Intepirdine is administered orally at either 35mg or 70mg once daily.

Intepirdine does not currently have Marketing Authorisation in the EU for any indication. Intepirdine is in phase III clinical trials for mild to moderate Alzheimer’s disease in combination with donepezil.

INNOVATION and/or ADVANTAGES

If licensed, intepirdine will offer an additional treatment option for dementia with Lewy bodies.

DEVELOPER

Axovant Sciences Ltd.

AVAILABILITY, LAUNCH OR MARKETING

In phase II clinical trials.

PATIENT GROUP

BACKGROUND

Dementia is a chronic progressive mental disorder, which is largely irreversible and characterised by a widespread impairment of mental function. It adversely affects higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgement.

The symptoms of dementia with Lewy bodies usually develop gradually becoming more severe over the course of a few years. People with dementia with Lewy bodies may have specific symptoms that can help distinguish it from other types of dementia, including extreme swings between alertness, confusion and drowsiness; slow movement, stiff limbs and tremors (as seen in Parkinson's disease); hallucinations; fainting, unsteadiness and falls; sleep disturbances; loss of facial expression; dysphagia and depression.

CLINICAL NEED and BURDEN OF DISEASE

Dementia with Lewy bodies is a common form of dementia estimated to affect more than 100,000 people in the UK. Dementia with Lewy bodies accounts for 4% of all recorded
dementia, but there is good evidence that the condition is not always diagnosed correctly. Based on studies of brain tissue after death, scientists think dementia with Lewy bodies may account for as much as 10-15% of all dementia\(^5\).

The rate of disease progression and life expectancy varies; on average, someone might live for about 6-12 years after the first symptoms\(^5\).

The population likely to be eligible to receive intepirdine could not be estimated from available published sources.

**PATIENT PATHWAY**

**RELEVANT GUIDANCE**

**NICE Guidance**

- NICE guidelines. Older people with social care needs and multiple long-term conditions (NG22). November 2015.

**NHS England Policies and Guidance**

CURRENT TREATMENT OPTIONS

There is no cure for dementia with Lewy bodies and there are currently no medications that slow progression.

Acetylcholinesterase inhibitors such as donepezil, galantamine or rivastigmine (which are licensed for mild to moderate dementia in Alzheimer’s disease, but unlicensed for dementia with Lewy bodies) have been shown to improve symptoms such as hallucinations, confusion and drowsiness in some people\(^6,8\).

Treatment aims to promote independence, maintain function and treat symptoms, including non-cognitive (such as hallucinations, delusions, anxiety, marked agitation and associated aggressive behaviour), cognitive, behavioural and psychological symptoms\(^2\). Non-pharmacological management options include: social support, increasing assistance with day-to-day activities, information and education, carer support groups, community dementia teams, home nursing and personal care, community services such as meals-on-wheels, befriending services, day centres, respite care, care homes, physiotherapy, and speech and language therapy\(^2,4,9\).

EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>The HEADWAY-DLB Study, NCT02669433, RVT-101-2001; aged 50-85 yrs; intepirdine vs placebo; phase Iib.</th>
<th>NCT02928445, RVT-101-2002; aged 50-86 yrs; intepirdine; phase II extension.</th>
<th>NCT02910102, RVT-101-2003; adults aged 50-89 yrs; intepirdine vs placebo; phase II.</th>
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<tbody>
<tr>
<td>Sponsor</td>
<td>Axovant Sciences Ltd.</td>
<td>Axovant Sciences Ltd.</td>
<td>Axovant Sciences Ltd.</td>
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<tr>
<td>Source of information</td>
<td>Trial registry(^1).</td>
<td>Trial registry(^10).</td>
<td>Trial registry(^11).</td>
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<tr>
<td>Location</td>
<td>USA, France and Spain.</td>
<td>USA, France and Spain.</td>
<td>USA.</td>
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<tr>
<td>Participants</td>
<td>n=240 (planned); aged 50-85 yrs; probable dementia with Lewy bodies; Mini Mental State Examination (MMSE) score 14-26; reliable caregiver who is willing to report on the subject’s status.</td>
<td>n=240 (planned); aged 50-86 yrs; pts that have completed last on-treatment visit of the HEADWAY Study.</td>
<td>n=40 (planned); aged 50-89 yrs; a clinical diagnosis of Alzheimer’s disease; MMSE score 14-26; gait impairment; stable background acetylcholinesterase inhibitor therapy.</td>
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<tr>
<td>Schedule</td>
<td>Randomised to intepirdine 35mg or 70mg; or placebo; oral once daily.</td>
<td>Pts previously randomised to placebo receive intepirdine 70mg. Pts previously randomized to intepirdine will continue in the same treatment arm.</td>
<td>Randomised to intepirdine 35mg; or placebo; oral once daily.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment 24 wks, follow-up 24 wks.</td>
<td>Active treatment 24 wks, follow-up 24 wks.</td>
<td>Active treatment 12 wks, follow-up 12 wks.</td>
</tr>
</tbody>
</table>
**Primary outcome/s**
Clinician’s Interview-Based Impression of Change Plus Caregiver Input (CIBIC+); computerised cognitive battery.

**Adverse events (AEs); change in physical examinations, vital signs, electrocardiograms (ECGs), and clinical laboratory assessments.**

**Secondary outcome/s**
Clinical assessment of visual hallucinations; EQ-5D; AEs.

AEs. No quality of life measurement included in trial outcomes.

**Expected reporting date**
Estimated primary completion date October 2017.

Estimated primary completion date March 2018.

Estimated primary completion date September 2017.

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**ESTIMATED COST and IMPACT**

**COST**

The cost of intepirdine is not yet known.

**IMPACT - SPECULATIVE**

**Impact on Patients and Carers**
- Reduced mortality/increased length of survival
- Other

- Reduced symptoms or disability
- No impact identified

**Impact on Health and Social Care Services**
- Increased use of existing services
- Re-organisation of existing services
- Other

- Decreased use of existing services
- Need for new services
- None identified

**Impact on Costs and Other Resource Use**
- Increased drug treatment costs
- Other increase in costs.

- Reduced drug treatment costs
- Other reduction in costs
- None identified

**Other Issues**
- Clinical uncertainty or other research question identified

- None identified

**REFERENCES**


