Lay summary

VTS-270 is a new drug that is injected into the spine to treat Neimann-Pick disease, which is a rare genetic disorder that causes accumulation of fats in cells throughout the body, including the liver and the brain. It may lead to balance and learning difficulties and most patients do not survive beyond age 25. Some studies have suggested that VTS-270 may help patients with Neimann-Pick disease to have better quality of life.

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.

This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.
TARGET GROUP

- Niemann-Pick disease type C1 (NPC1).

TECHNOLOGY

DESCRIPTION

VTS-270 (Kleptose; 2-Hydroxypropyl-beta-cyclodextrin; HP-beta-CD; HPBCD) is a mixture of 2-hydroxypropyl-B-cyclodextrins with a specific compositional fingerprint for the treatment of NPC1. VTS-270 may prevent cerebellar dysfunction and Purkinje cell death\(^1\). In Part A of a phase II/III clinical trial, VTS-270 was administered via lumbar intrathecal (IT) injection at doses of 900mg, 1200mg, and 1800mg every 2 weeks for 8 weeks\(^2\).

VTS-270 does not currently have Marketing Authorisation in the EU for any indication. It is not in clinical trials for any other indications.

INNOVATION and/or ADVANTAGES

If licensed, VTS-270 will offer an additional treatment option for patients with Niemann-Pick type C1 disease, a group who currently have few effective therapies available.

DEVELOPER

Vtesse Inc.

AVAILABILITY, LAUNCH OR MARKETING

VTS-270 is a designated orphan drug in the EU and USA for Niemann-Pick disease type C (NPC).

VTS-270 was awarded Promising Innovative Medicine (PIM) designation for NPC by the MHRA in Jan 2017.

PATIENT GROUP

BACKGROUND

NPC is a lysosomal storage disease that is transmitted in an autosomal recessive manner and is caused by mutations in either the NPC1 gene (in 95% of cases) or the NPC2 gene (in around 5% of cases)\(^3,4\). These mutations impair the processing and utilisation of cholesterol leading to intracellular accumulation of unesterified cholesterol\(^5\). NPC has a wide clinical spectrum, typically causing splenomegaly, hepatomegaly and progressive neurological disease, which is responsible for the morbidity and premature mortality associated with the disease. Other symptoms include dysarthria, dystonia, ataxia, cataplexy, tremors and/or seizures, dysphagia, and difficulty in up- and downward eye movement\(^4\). The age of onset and rate of disease progression varies greatly from person to person\(^4\).
CLINICAL NEED and BURDEN OF DISEASE

NPC has an estimated minimum incidence of 1 in 120,000 live births\(^5\). The true incidence and prevalence of NPC is difficult to assess, because of insufficient clinical awareness combined with the relative difficulty of biochemical testing. Estimates of birth prevalence ranging between 0.66 and 0.83 per 100,000 were proposed for France, the UK and Germany based on diagnoses made in one laboratory over the period 1988-2002\(^6\). Although rate of disease progression and life expectancy vary, the majority of patients die between the ages of 10 and 25 years\(^3\).

In 2014-15, there were 630 admissions for other sphingolipidosis (ICD-10 E75.2) in England, resulting in 869 bed days and 654 finished consultant episodes\(^6\).

The population likely to be eligible to receive VTS-270 could not be estimated from available published sources.

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance

- No relevant guidance identified.

NHS England Policies and Guidance


Other Guidance


CURRENT TREATMENT OPTIONS

There is no cure for NPC and patient management largely comprises symptom control\(^4,5\). Miglustat is the only approved drug for the treatment of progressive neurological deterioration in children and adults with NPC\(^3,4,5\). The correct identification and application of disease specific therapies as early as possible can improve quality of life\(^3\). Examples of measures for symptom control include\(^3\):

- Dysphagia: patients should be monitored for dysphagia and measures such as softening or thickening of food and gastrostomy should be considered.
- Sialorrhoea: botulinum toxin may be used to reduce drooling.
Cataplexy: tricyclic antidepressants or central nervous system stimulants may help reduce cataplexy.
Sleep disturbances: melatonin or positive airway pressure may help.

**EFFICACY and SAFETY**

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT02534844, VTS301, EUCTR2015-002548-15-DE; VTS-270 vs placebo; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Vtesse Inc.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry².</td>
</tr>
<tr>
<td>Location</td>
<td>EU (incl UK), USA, Australia and Turkey.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=51 (planned); aged 4-21 yrs; NPC1; onset of neurological symptoms &gt;15 yrs of age; total NPC Clinical Severity Scale Score ≥10; if taking miglustat, must be on stable dose for at least 3 mths and continue to do so. Potential participants excluded if body weight ≤15kg, wheelchair bound, require nasogastric tube, have severe dysmetria or cognition NPC score=5. No prior treatment with intravenous 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) for NPC1 disease, unless the subject has undergone a minimum 3-mth washout period prior to study.</td>
</tr>
</tbody>
</table>
| Schedule      | Part A: subjects to receive VTS-270 via lumbar IT injection at one of three doses (900mg, 1200mg, and 1800mg) every 2 wks for 8 wks, or placebo, IT.  

Part B: subjects randomised to receive VTS-270 via lumber IT injection (dose to be confirmed following Part A) every 2 wks, or placebo sham, lumbar IT injection every 2 wks.  

Part C: open-label extension, participants receive VTS-270 via lumbar IT injection every 2 wks. |
| Follow-up     | Active treatment in the placebo-controlled Part B for up to 52 wks.         |
| Primary outcome/s | NPC Clinical Severity Score.                                           |
| Secondary outcome/s | Clinician and Caregiver Clinical Global Impression of Change; time to get up and go test; 9-hole peg test; percentage of pts with clinical worsening; European Quality of Life-5 Dimensions Quality of Life Rating (EQ-5D QoL); cerebrospinal fluid and plasma protein biomarkers. |
| Expected reporting date | Study completion date reported as Mar 2018. |

**ESTIMATED COST and IMPACT**

**COST**

The cost of VTS-270 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: *fortnightly intrathecal administration*
- Decreased use of existing services
- Re-organisation of existing services
- Need for new services
- Other:
- 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 existing treatments.*
- None identified

#### Other Issues
- Clinical uncertainty or other research question identified:
- None identified

### REFERENCES

5. Vanier MT. Niemann-Pick disease type C. Orphanet Journal of Rare Diseases 2010;5:16.