

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Highly Specialised Technologies Evaluation**

**Givosiran for treating acute hepatic porphyria [ID1549]**

**Final scope**

**Draft remit/appraisal objective**

To evaluate the benefits and costs of givosiran within its marketing authorisation for treating acute hepatic porphyria for national commissioning by NHS England.

**Background**

Acute hepatic porphyrias (AHPs) are a group of rare inherited metabolic disorders caused by the deficiency of one of the enzymes needed to create haem. Haem is formed of porphyrin, which is created from precursors including delta-aminolevulinic acid (ALA) and porphobilinogen (PBG). In AHP, these precursors to porphyrin accumulate in the liver and other tissues. Four types of porphyria are classed as acute: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP) and aminolevulinic acid dehydratase porphyria (ADP). AIP is the most common form of AHP in the UK and has the highest symptom burden.<sup>1</sup>

The accumulation of precursors of porphyrin damages nerve cells and can provoke acute attacks of physical pain. AHP is life-threatening as it can lead to seizures, paralysis and respiratory arrest during acute attacks and it is debilitating in the long-term because of symptoms such as chronic pain, fatigue, nausea and vomiting. In addition, HCP and VP are associated with damage to the skin through sun exposure.<sup>1</sup> Acute attacks are very rare before puberty and usually start between 15 and 35 years old and they are more common in women.<sup>2</sup> There may be an increased risk of having an acute attack during or following pregnancy.<sup>1</sup> Acute attacks are often triggered by exogenous factors such as drugs, alcohol, endocrine factors, and infection.<sup>2</sup>

The prevalence of AHP is estimated to be 0.1 in 10,000 people<sup>3</sup> in the general European population which is equivalent to around 560 patients in England.<sup>4</sup> Most people have one or a few attacks followed by full recovery but in around 10% of cases, acute attacks are recurrent. According to the National Acute Porphyria Service, there are currently 35 people receiving treatment for severe recurrent acute attacks in the UK.

Current treatment options for AHP aim at eliminating or managing symptoms and includes pain management, stopping of medications that could have triggered the symptoms, gonadotrophin analogues for hormonally induced attacks and oral or intravenous glucose (for treatment of an acute attack).<sup>1,5</sup> Haem arginate (human hemin) is indicated for the treatment of acute attacks of AHP. It is sometimes used outside of its marketing authorisation to prevent

the attacks. Liver transplantation may be an option for some people with severe recurrent acute attacks when other treatment options have not worked.

**The technology**

Givosiran (Givlaari, Alnylam) is a ribonucleic acid interference agent that suppresses the production of delta-aminolevulinic acid synthase 1 (ALAS1) by the liver in order to reduce the accumulation of the precursors of porphyrin. It is administered by subcutaneous injection.

Givosiran has a marketing authorisation in the UK for treating acute hepatic porphyria in adults and adolescents aged 12 years or older.

<b>Intervention(s)</b>	Givosiran
<b>Population(s)</b>	Adults and young people aged 12 years or older with recurrent severe attacks of acute hepatic porphyria
<b>Comparators</b>	Established clinical management without givosiran, which may include: <ul style="list-style-type: none"> <li>• haem arginate</li> <li>• gonadotrophin analogues</li> <li>• liver transplantation</li> </ul>
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• numbers of acute attacks</li> <li>• porphyrin precursor concentrations in urine</li> <li>• neurological impairment</li> <li>• autonomic function</li> <li>• mortality</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life (for patients and carers).</li> </ul>
<b>Nature of the condition</b>	<ul style="list-style-type: none"> <li>• disease morbidity and patient clinical disability with current standard of care</li> <li>• impact of the disease on carer’s quality of life</li> <li>• extent and nature of current treatment options</li> </ul>

<b>Clinical effectiveness</b>	<ul style="list-style-type: none"> <li>• overall magnitude of health benefits to patients and, when relevant, carers</li> <li>• heterogeneity of health benefits within the population</li> <li>• robustness of the current evidence and the contribution the guidance might make to strengthen it</li> <li>• treatment continuation rules (if relevant)</li> </ul>
<b>Value for Money</b>	<ul style="list-style-type: none"> <li>• cost effectiveness using incremental cost per quality-adjusted life year</li> <li>• patient access schemes and other commercial agreements</li> <li>• the nature and extent of the resources needed to enable the new technology to be used</li> </ul>
<b>Impact of the technology beyond direct health benefits</b>	<ul style="list-style-type: none"> <li>• whether there are significant benefits other than health</li> <li>• whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services</li> <li>• the potential for long-term benefits to the NHS of research and innovation</li> <li>• the impact of the technology on the overall delivery of the specialised service</li> <li>• staffing and infrastructure requirements, including training and planning for expertise.</li> </ul>
<b>Other considerations</b>	<ul style="list-style-type: none"> <li>• Guidance will only be issued in accordance with the marketing authorisation.</li> <li>• Guidance will take into account any Managed Access Arrangements.</li> </ul>
<b>Related NICE recommendations and NICE Pathways</b>	None
<b>Related National Policy</b>	<p>NHS England (2018/2019) Manual for prescribed specialised services, service 99: Severe acute porphyria service (adults and children)</p> <p><a href="https://www.england.nhs.uk/publication/manual-for-prescribed-specialised-services/">https://www.england.nhs.uk/publication/manual-for-prescribed-specialised-services/</a></p>

	<p>NHS England (2018) Highly Specialised Services Highlight report: Severe acute porphyria service (adults and children) <a href="https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2018/12/Highly-Specialised-Services-2018-v2.pdf">https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2018/12/Highly-Specialised-Services-2018-v2.pdf</a></p> <p>Department of Health and Social Care, NHS Outcomes Framework 2017-2018 (published 2016): Domains 1, 2, 3, 4 and 5. <a href="https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf">https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf</a></p>
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### References

- 1 British Liver Trust (2008) Porphyria. Fighting the disease.  
[http://www.britishlivertrust.org.uk/wp-content/uploads/PPH0208\\_lores.pdf.pdf](http://www.britishlivertrust.org.uk/wp-content/uploads/PPH0208_lores.pdf.pdf). Accessed July 2020
- 2 European Porphyria Network (2018) [The porphyrias](#). Accessed July 2020
- 3 European Medicines Agency (2016) Public summary of opinion on orphan designation [P https://www.ema.europa.eu/documents/orphan-designation/eu/3/16/1731-public-summary-opinion-orphan-designation-synthetic-double-stranded-sirna-oligonucleotide\\_en.pdf](https://www.ema.europa.eu/documents/orphan-designation/eu/3/16/1731-public-summary-opinion-orphan-designation-synthetic-double-stranded-sirna-oligonucleotide_en.pdf). Accessed July 2020
- 4 Office for National Statistics. [Population Estimates for UK, England and Wales, Scotland and Northern Ireland: mid-2018](#). Accessed July 2020
- 5 [NHS Standard Contract for Severe Acute Porphyria](#) (2013/14). Accessed July 2020