NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Metreleptin for treating lipodystrophy

Final scope

Remit

To evaluate the benefits and costs of metreleptin within its licensed indication for treating lipodystrophy for national commissioning by NHS England.

Background

Lipodystrophy is a rare, heterogeneous group of syndromes characterised by the complete or partial loss or absence of subcutaneous adipose tissue. Without sufficient adipose tissue the hormone leptin can become deficient and the body's system for regulating energy use and storage is disrupted, resulting in lipid accumulation in abnormal sites, such as the liver and muscle. Lipodystrophy is often accompanied by metabolic abnormalities including insulin resistance with resultant hyperinsulinemia and diabetes mellitus, hepatic steatosis or steatohepatitis, dyslipidemia and severe hypertriglyceridemia. It can therefore have a substantial effect on quality of life. Despite progress in identifying the molecular basis of many lipodystrophy syndromes, it is often diagnosed late in the course of the disease or remain undiagnosed.

Lipodystrophy is generally classified on the basis of the extent or pattern of fat loss (generalised or partial) and whether the disease is genetic or acquired. There are 4 major subtypes:

Generalised:

- congenital (inherited) generalised lipodystrophy
- acquired generalised lipodystrophy

Partial:

- familial partial (inherited) lipodystrophy
- acquired partial lipodystrophy

The prevalence of lipodystrophy varies from approximately 1 to 2 per 1,000,000 population depending on the subtype. Applying the prevalence estimates to the population of England for 2016[1] suggests there are approximately 200 people with lipodystrophy in England.

There are no licensed treatments in the UK for generalised or partial lipodystrophy. The disease is currently managed with lifestyle modifications: such as a low fat diet and exercise; cosmetic surgery; and medications to manage the metabolic disturbance associated with leptin deficiency, including lipid lowering drugs (fibrates and statins) and medications for diabetes

(metformin, insulin, sulphonylureas, and thiazolidinediones). A single National Specialist Service for people with lipodystrophy was established in 2011 at Addenbrooke's Hospital in Cambridge.

The technology

Metreleptin (Myalept, Aegerion Pharmaceuticals) is an analogue of the human hormone leptin, which is secreted into the circulation from adipocytes. Leptin acts centrally through multiple metabolic actions within the arcuate nucleus to affect body composition, appetite and metabolism. Metreleptin is administered by subcutaneous injection.

Metreleptin does not currently have a marketing authorisation in the UK for treating lipodystrophy. It has been studied in clinical trials in people with generalised or partial lipodystrophy.

Intervention(s)	Metreleptin
Population(s)	People with generalised or partial lipodystrophy
Comparators	Established clinical management without metreleptin (including diet and lifestyle modifications, lipid lowering drugs and medications for diabetes)
Outcomes	The outcome measures to be considered include: • improvement in metabolic abnormalities • liver function (including cirrhosis) • glucose control and diabetes (including complications of diabetes and need for diabetes therapies) • satiety • pancreatitis • use of other drugs • organ damage including heart and kidneys • growth and development • reproductive dysfunction • infection • mortality • adverse effects of treatment • health-related quality of life (for patients and carers; including effects on appearance)
Nature of the	• disease morbidity and patient clinical disability

condition	with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options
Clinical Effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• Cost effectiveness using incremental cost per quality-adjusted life year • Patient access schemes and other commercial agreements • The nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.

Other considerations	• If the evidence allows, subgroups according to whether the lipodystrophy is generalised or partial, or congenital or acquired, and according to the presence of complications associated with lipodystrophy (including diabetes and hypertriglyceridemia) will be considered. • Guidance will only be issued in accordance with the marketing authorisation. • Guidance will take into account any Managed Access Arrangements
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England, Manual for prescribed specialised services 2016/17, Chapter 62: Highly specialist metabolic disorder services (adults and children), 2016 https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf National Service Frameworks: Long Term Conditions (including neurological) – archived http://webarchive.nationalarchives.gov.uk/+/www.nhs.uk/NHSEngland/NSF/Pages/Longtermconditions.aspx Department of Health NHS outcomes framework 2016 to 2017 (2016) https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

[1] Population of England (2016) https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates Accessed October 2017