NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Metreleptin for treating lipodystrophy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of metreleptin within its marketing authorisation for treating lipodystrophy.

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.

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 0.05 to 1 person per 100,000 population[1] depending on the subtype. Applying the prevalence rates to the population of England for 2015[2] suggests there are approximately 712 people with lipodystrophy in England (82 people with generalised lipodystrophy and 630 people with partial lipodystrophy).

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 2012 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 lifestyle modifications, lipid lowering drugs and medications for diabetes)
Outcomes	The outcome measures to be considered include: • improvement in metabolic abnormalities • glucose and lipid control • mortality • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	If the evidence allows, subgroups according to whether the lipodystrophy is generalised or partial, or congenital or acquired, will be considered. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
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

Questions for consultation

Have all relevant comparators for metreleptin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for generalised and partial lipodystrophy? In what settings would lipodystrophy be managed in the NHS?

Is the population defined appropriately?

- Will metreleptin be considered for generalised and/or partial lipodystrophy?
- Would metreleptin be considered for people with HIV related lipodystrophy?

How many people would be expected to be considered for metreleptin treatment in clinical practice in England?

Are the outcomes listed appropriate? Do they capture the most important aspects of metreleptin treatment for people with lipodystrophy? Should any other outcomes be included?

Are the subgroups suggested in `Other considerations` appropriate? Are there any other subgroups of people in whom metreleptin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which metreleptin will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider metreleptin to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of metreleptin can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

[1] European Medicines Agency (2014) `Public summary of opinion on orphan designation: metreleptin for the treatment of Barraquer-Simons syndrome`http://www.ema.europa.eu/docs/en_GB/document_library/Orphan_designation/2012/08/WC500131630.pdf Accessed October 2016.

[2] Population of England (2015) https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates Accessed October 2016