Highly Specialised Technologies (HST) criteria checklist

Pegunigalsidase alfa for treating Fabry disease [ID3904]

### Introduction

The NICE HST criteria checklist is to highlight where a technology meets/partially meets or does not meet the criteria for routing to the HST programme. Its purpose is to show the details of why a technology may not be appropriate for HST evaluation, but also where it has been identified as suitable. For more information, please see [section 7 of NICE health technology evaluation topic selection: the manual](https://www.nice.org.uk/process/pmg37/chapter/highly-specialised-technologies)

### Key – Please use the colour key to advise if the technology meets the criteria

|  |  |
| --- | --- |
| Met  | There is clear and strong evidence that the criterion is met |
| Unclear | There is some evidence, or the evidence available is unclear that the criterion is met. |
| Not met | There is no evidence or limited evidence that the criterion is met.  |

### MA wording: xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx.

| **Number** | **Criterion** | **Description of how the technology meets the criteria**  | **Does the technology meet the criteria?** |
| --- | --- | --- | --- |
|  | The disease is very rare defined by 1:50,000 in England  | Prevalence of symptomatic Fabry is estimated to be 1 in 49,000.[[1]](#endnote-1)Would be higher if asymptomatic and presymptomatic people were included (such as those with late-onset disease, or females who have an additional copy of the GLA gene which compensates for the mutation). Newborn screening has estimated that the incidence of Fabry may be 1 in 4,000 males (but not all would become symptomatic/receive treatment) – unknown prevalence in females.[[2]](#endnote-2) | Unclear |
|  | Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications  | Estimates for prevalence vary, but best quality data suggests number of adults in England with Fabry:* ~1,173 (based on data collected by MPS Society 2022)[[3]](#endnote-3)
* ~1,000 (symptomatic, based on prevalence of 1 in 49,000 x 2020 England population, assumption of 90% adults).1,[[4]](#endnote-4)

Not all of these people would immediately start treatment. Depends on severity and progression.[[5]](#endnote-5) Best estimates suggest:* Adults on treatment in England; ERT or migalastat: 428 (NHS 2019)[[6]](#endnote-6)
* Adults on ERT in England:

NHS 2019: 3476MPS Society 2022: 4273 | Not met |
|  | The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life  | Fabry disease is a lifelong, progressive condition caused by alterations (mutations) in the alpha-galactosidase A (GLA) gene located on the X-chromosome. It is associated with a wide range of symptoms and affects several organs. It can lead to heart and renal failure and can raise a patient’s risk of stroke.Life expectancy estimated at 66.5 in HST4 modelling.[[7]](#endnote-7)Waldek et al. 2009 from USA found:males 58.2 years vs. 74.7 years in general population females 75.4 years vs. 80 years in general population[[8]](#endnote-8)Clinical expert said these figures are reflective of current life expectancy in the UK.However, given the first enzyme replacement therapy for Fabry disease was approved in 2003, this data may not reflect the full impact that enzyme replacement therapy could have on life expectancy (i.e. life expectancy may be expected to increase over time as more people have had treatments from an earlier age).  | Met |
|  | There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options. | Two existing enzyme replacement therapies are available; agalsidase alpha and agalsidase beta (both administered via IV infusion). Migalastat is also available as alternative to ERT for those with an amenable mutation (oral therapy).Clinical input during the scoping workshop confirmed these existing treatments have important clinical benefits (improving symptom control and slowing disease progression). They are widely used and ‘best supportive care’ was removed as a comparator during the scoping consultation process because the clinical experts confirmed it was not used in NHS practice.Despite the benefits of treatment, clinical input during scoping workshop confirmed the impact of treatment has “not been transformational” and unmet needs remain. Patients may still suffer from debilitating symptoms (pain, GI problems), organ damage and shortened life expectancy. Pegunigalsidase alpha is an enzyme replacement therapy so has the same mechanism of action as agalsidase alpha and agalsidase beta (albeit with some expected benefits from pegylation). Although pegunigalsidase alfa is expected to offer some benefits over existing therapies, these are not expected to be significant. The expected benefits include:* Less frequent dosing schedule (monthly vs. fortnightly)
* Reduced immunogenicity
* Fewer infusion related reactions

In the BALANCE study, pegunigalsidase was shown to be non-inferior to agalsidase beta for the primary endpoint of kidney function (eGFR Slope), which is a key measure of Fabry disease progression.[[9]](#endnote-9)  | Not met |

1. . Brennan, P. and Parkes, O. (2014) Case-finding in Fabry disease: experience from the North of England. Journal of inherited metabolic disease, 37 (1): 103–107 [↑](#endnote-ref-1)
2. . Gragnaniello, V., et al. (2021) Newborn Screening for Fabry Disease in Northeastern Italy: Results of Five Years of Experience. Biomolecules, 11(7), 951. [↑](#endnote-ref-2)
3. . MPS Society May 2022. Adult Fabry patients in England. (Data on file) [↑](#endnote-ref-3)
4. . Office for National Statistics, 2020 mid-year estimate for England population [↑](#endnote-ref-4)
5. . BIMDG (2020) Guidelines for the Treatment of Fabry Disease.. Available online: [**https://bimdg.org.uk/store/lsd//FabryGuide\_LSDSS\_Jan2020\_700523\_11032020.pdf**](https://bimdg.org.uk/store/lsd/FabryGuide_LSDSS_Jan2020_700523_11032020.pdf)  [↑](#endnote-ref-5)
6. . NHS England (2019) Fabry patients treated in England. (Data on file) [↑](#endnote-ref-6)
7. . Migalastat for treating Fabry disease. Highly specialised technologies guidance. Published: 22 February 2017 www.nice.org.uk/guidance/hst4 [↑](#endnote-ref-7)
8. . Waldek, S., Patel, M. R., Banikazemi, M., Lemay, R., & Lee, P. (2009). Life expectancy and cause of death in males and females with Fabry disease: findings from the Fabry Registry. Genetics in Medicine, 11(11), 790-796. [↑](#endnote-ref-8)
9. . Protalix BioTherapeutics and Chiesi Global Rare Diseases Announce Topline Results from the 24-Month Phase III BALANCE Clinical Trial of PRX-102 for the Treatment of Fabry Disease. <https://www.chiesi.com/en/protalix-biotherapeutics-and-chiesi-global-rare-diseases-announce-topline-results-from-the-24-month-phase-iii-balance-clinical-trial-of-prx-102-for-the-treatment-of-fabry-disease/> Accessed July 2022 [↑](#endnote-ref-9)