

18 March 2024

Dr Mark Chakravarty

Lead Non-executive Director NICE Appeals – Technology Appraisals and Highly Specialised Technologies

National Institute for Health and Care Excellence 2nd Floor

2 Redman Place London E20 1JQ

Dear Dr Chakravarty,

**Re: Final Appraisal Determination –** Olipudase alfa for treating Niemann-Pick disease types A and B [ID3913]

We are writing this letter to appeal the NICE final draft guidance on olipudase alfa for treating Niemann-Pick disease types A and B [ID3913] on the grounds that NICE has failed to act fairly. We set out our points of appeal below.

Ground 1 (a): the decision not to recommend treatment with olipudase alfa is unfair on patients with Niemann-Pick disease type B because similar enzyme replacement therapies for other lysosomal storage disorders which are less cost effective have received positive recommendations. We believe that NICE is using entirely different criteria to assess novel treatments for diseases where no disease modifying therapy is available, to those criteria they are

using to assess new therapies for diseases where other licensed treatment options already exist.

The Highly Specialised Technology committee which assessed olipudase alfa agreed that this is a highly effective therapy for Niemann-Pick disease type B (NPB). They agreed that the technology met the criteria for a 1.5% discount rate to be applied rather than the preferred 3.5% rate. They determined that treatment would lead to a substantial gain of 27.6 QALYs and applied a full QALY weighting of 2.7.

Despite this favourable treatment, the company and NHS England were unable to agree on a price for olipudase alfa which would produce an ICER of less than

£300,000 per QALY gained, and therefore treatment with olipudase alfa could not be recommended.

Given that the company could not have expected the committee to be more generous in its discount rate and QALY weighting, it is disappointing that they were

not prepared to offer olipudase alfa at an appropriate price. This may be because their expectations for the price they could obtain were based on the fact that NICE has recently recommended other enzyme replacement therapies (ERTs) for different lysosomal storage disorders (LSDs) which are considerably less clinically and cost effective.

Avalglucosidase alfa and cipaglucosidase alfa with miglustat have both recently been recommended for treatment of late onset Pompe disease in adults and pegunigalsidase alfa has been recommended for treatment of Fabry disease. All three of these ERTs went through a standard technology appraisal process rather than a highly specialised technology evaluation process. They are all extremely expensive drugs (BNF prices suggest that the annual cost of treating a 70 kg patient would be approximately £285,000 for avalglucosidase alfa, £336,000 for cipaglucosidase alfa with miglustat and £111,000 for pegunigalsidase alfa - although the NHS does get a confidential discount) and it is not conceivable that they could have an ICER of less than £20,000 per QALY, as is clearly stated in the committee discussion for all three products. How then did the committee reach its decision to recommend them for use in the NHS?

For Pompe and Fabry disease, the NHS ‘standard of care’ involves treatment with drugs which have never been through NICE processes, or any NHSE costeffectiveness assessment. When new technologies for these conditions are assessed, the process which NICE uses makes no attempt to assess their actual cost-effectiveness but instead generates an ICER which simply compares the costeffectiveness of the new treatment with that of the currently available, standard of care treatment. If a company can demonstrate that their product is non-inferior to an

existing therapy, and offer it at a similar or lower price, they will receive a positive recommendation without any assessment of the actual cost per QALY having been made.

Even if it seems unlikely that these drugs would meet the £20,000 per QALY threshold for a standard technology appraisal, might they not come in under the

£300,000 per QALY threshold for a Highly Specialised Technology evaluation, even though they were not assessed under those criteria? They were all approved on the basis that they were non-inferior, rather than superior, to the existing standard of care therapies and therefore their cost-effectiveness is likely to be similar.

Although NICE has never assessed the cost effectiveness of ERT for Pompe or Fabry disease, other assessments have been made and published. A Dutch group have assessed the cost effectiveness of ERT for adult patients with Pompe disease (Kanters TA *et al*, Cost-effectiveness of enzyme replacement therapy with alglucosidase alfa in adult patients with Pompe disease. Orphanet J Rare Dis. 2017 Dec 13;12(1):179). They concluded that the treatment produced significant improvements in survival (from 1.9 years to 5.4 years depending on the scenario used) and patients’ quality of life. However, the incremental cost per QALY was between €1.8 million and €3.2 million. The NHS would need to receive an 80-90% discount to make this treatment approach NICE thresholds for cost-effectiveness. It

therefore seems extremely unlikely that NICE would recommend any of the currently available ERTs for use in adults with late onset Pompe disease if they were put through a full Highly Specialised Technology appraisal, and yet avalglucosidase alfa and cipaglucosidase alfa have both been approved under a standard technology appraisal.

The situation for Fabry is even more stark. The best available assessment of the cost-effectiveness of ERT in Fabry disease (Rombach S *et al*, Cost-effectiveness of enzyme replacement therapy for Fabry disease. Orphanet J Rare Dis. 2013 Feb 19;8:29) showed that treatment produces a modest gain in QALYs (1.7 in males, 1.4 in females) at an undiscounted cost of £4.8 - 6.6 million per QALY. It seems inconceivable that pegunigalsidase alfa, or any other currently available disease modifying therapy for Fabry, could ever meet any NICE threshold for cost effectiveness, but it has nonetheless received a positive recommendation from a standard technology appraisal.

Olipudase alfa is clearly much more clinically effective than any ERT for late onset Pompe or Fabry disease. It can reverse the clinical features of the disease, and the NICE appraisal suggested a lifetime gain of 27.6 QALYS. At BNF prices, it would cost £986,000 per year to treat a 70 kg adult. This is significantly more than the same costs for a patient with Pompe or Fabry receiving ERT, but olipudase alfa is also much more effective than ERT for Pompe and Fabry. The cost per QALY of treating a patient with NP-B with olipudase alfa will still be very high, but much more favourable than that for avalglucosidase alfa or cipaglucosidase alfa with miglustat in adults with Pompe, or of pegunigalsidase alfa in patients with Fabry.

The examples we give here make it clear that NICE is using entirely different criteria to assess novel treatments for diseases where no disease modifying therapy is available to those they are using to assess new therapies for diseases where other licensed treatment options already exist. This is extremely unfair and disadvantageous to patients with conditions such as NP-B, who cannot access a lifetransforming treatment whilst at the same time NICE mandates the NHS to provide drugs which are much less cost-effective for similar conditions. Because of this

differential approach to appraising drugs, depending on whether another licensed treatment is already available and regardless to whether that treatment has been subjected to a rigorous assessment of its cost-effectiveness, NHSE is not obtaining value for money from its expenditure on these high-cost drugs and patients are being unfairly deprived of a life-saving treatment.

The appellant would like to be heard at an oral appeal should one take place.

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Consultant in Inherited Metabolic Disease

University College London Hospitals NHS Foundation Trust

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