NICE National Institute for Health and Care Excellence

NICE guidance

Cipaglucosidase alfa with miglustat for treating late-onset Pompe disease

Technology appraisal guidance
Published: 15 August 2023

www.nice.org.uk/guidance/ta912

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Cipaglucosidase alfa (CIPA) plus miglustat is recommended, within its marketing authorisation, as an option for treating late-onset Pompe disease in adults. It is recommended only if the company provides it according to the commercial arrangement.

Why the committee made these recommendations

The standard treatment for late-onset Pompe disease is enzyme replacement therapy (ERT) with alglucosidase alfa (ALGLU) or avalglucosidase alfa (AVAL). CIPA plus miglustat is an alternative ERT.

The results of clinical trials show that CIPA plus miglustat seems to improve walking and breathing compared with ALGLU in the short term, but the long-term effects are uncertain. CIPA plus miglustat has only been compared indirectly with AVAL. It appears to be as effective, but this is uncertain.

There are also uncertainties in the cost-effectiveness model. But, compared with AVAL and ALGLU, there is a positive net health benefit for CIPA plus miglustat. This implies that overall population health will be increased if CIPA plus miglustat is an available treatment option. So, considering the total annual costs of the treatment options and despite the uncertainties in the clinical-effectiveness results and the model, CIPA plus miglustat is recommended for routine use.

2 Information about cipaglucosidase alfa with miglustat

Marketing authorisation indication

2.1 Cipaglucosidase alfa (Pombiliti, Amicus Therapeutics Ltd) is indicated as 'a long-term enzyme replacement therapy used in combination with the enzyme stabiliser miglustat for the treatment of adults with late-onset Pompe disease (acid α-glucosidase [GAA] deficiency)'. Miglustat (Opfolda, Amicus Therapeutics Ltd) is indicated as 'an enzyme stabiliser of cipaglucosidase alfa long-term enzyme replacement therapy in adults with late-onset Pompe disease (acid α-glucosidase [GAA] deficiency)'.

Dosage in the marketing authorisation

2.2 The dosage schedules are available in the summary of product characteristics for cipaglucosidase alfa and the summary of product characteristics for miglustat.

Price

2.3 The list price of cipaglucosidase alfa is £987 per 105 mg vial (excluding VAT; company communication). The list price of miglustat is £116.69 per 4 capsules of 65 mg (excluding VAT; company submission).

2.4 The company for cipaglucosidase alfa has a commercial arrangement. This makes it available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The evaluation committee considered evidence submitted by Amicus Therapeutics, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of condition

3.1 Pompe disease is a rare, genetic, chronic and progressive metabolic disease. It results in severe disability and reduces life expectancy. It is caused by mutations in the gene that encodes the enzyme acid alpha-glucosidase (GAA), which is needed to break down glycogen into glucose. In Pompe disease, there is reduced or no GAA activity, so lysosomal glycogen accumulates in muscle cells causing irreversible muscle damage. Disease severity is influenced by the level of residual GAA activity. There is a range of phenotypes of Pompe disease, with differing age of onset, extent of organ involvement and rate of progression. The phenotypes can be classified into 2 broad subtypes: infantile-onset Pompe disease and late-onset Pompe disease (LOPD). For LOPD, symptom onset is after 12 months and can occur any time up to late adulthood. LOPD typically affects multiple systems and is characterised by progressive muscle weakness and respiratory involvement. As LOPD progresses, people may need to use a wheelchair and may need non-invasive or invasive ventilation. Respiratory failure is the leading cause of death. There is significant heterogeneity among people with LOPD, including time of symptom onset, time of diagnosis, symptom severity, rate at which the condition worsens and life expectancy. The patient experts both experienced a delay in being correctly diagnosed, with one having initially been diagnosed with muscular dystrophy. They noted that this experience is not uncommon and can lead to a delay in starting effective treatment. The committee concluded that LOPD has a severe effect on both quality and length of life.

Clinical management

Treatment options

3.2 There are 2 treatment options available for LOPD, alglucosidase alfa (ALGLU) and avalglucosidase alfa (AVAL). They are enzyme replacement therapies (ERTs) that work by replacing GAA in the bloodstream. GAA helps the body to break down glycogen and prevents its toxic buildup. Alongside ERT, people with LOPD need tailored supportive care from multidisciplinary teams of healthcare professionals. AVAL only became available in early 2023, so in the NHS, most LOPD is treated with ALGLU. The clinical expert explained that, typically, symptoms initially improve in people having ALGLU, particularly in the first 6 to 12 months before the treatment effect plateaus. Over time, the treatment effect wanes. The clinical expert said that, in their experience, the condition will worsen in about 50% of people after 3 to 5 years on treatment. This results in reduced muscle strength, mobility and lung function, which can have a significant effect on both quality and length of life. AVAL is the same enzyme as ALGLU but has a different delivery mechanism, which aims to get more enzyme into muscle cells. The clinical expert said that both AVAL and cipaglucosidase alfa (CIPA) plus miglustat appear to have a more stable treatment effect than ALGLU. But the long-term efficacy of these new treatments is unknown. They emphasised that, because of the degenerative nature of Pompe disease, stability (not getting worse) is a positive health outcome. The patient experts noted that small changes in muscle or respiratory function could lead to a large effect on quality of life. Breathing easier and feeling less tired could enable someone to continue working or have a drink without assistance when thirsty. It was also noted that some people are unable to tolerate a specific treatment because of allergic reactions or side effects. For example, 1 patient expert said that they had had post-infusion headaches and hives with ALGLU. A patient expert also highlighted a previous supply shortage of ALGLU, which was caused by manufacturing issues. Having alternative treatment options would mitigate the risk of similar issues occurring in the future. The committee concluded that, while there are 2 treatment options available for people with LOPD, the response to treatment is variable. Also, the response to ALGLU typically wanes over time. So, alternative treatment options are welcome for people with Pompe

disease, especially when there is clinical decline on current treatment.

CIPA plus miglustat

3.3 CIPA has a marketing authorisation for LOPD in adults. CIPA is an ERT administered intravenously with miglustat, which is an enzyme stabiliser that is taken orally. The clinical expert said that the data on CIPA plus miglustat suggested that it has benefits over ALGLU at 1 year. They noted that these benefits appeared to last for at least 2 years. But they noted that there was considerable uncertainty about this because of the lack of long-term comparative data. They also confirmed that CIPA plus miglustat has a similar side effect profile to the existing ERTs. One patient expert explained that their symptoms were initially misdiagnosed. When they eventually got a correct diagnosis for Pompe, they promptly started treatment with ALGLU. Following an initial improvement in their symptoms, their condition started to plateau after around 4 to 5 years, and then began to decline. Their lung function worsened, and they had muscle pain and several choking episodes because of muscle weakness. They enrolled on a clinical trial for CIPA plus miglustat and had improved lung function, no muscle pain and no further choking episodes. They also had improved speech, more stamina, less fatigue and no post-infusion headaches. They thought that the treatment benefit lasted for the full 2 weeks between infusions while, with ALGLU, they would begin to feel it wearing off after around 8 days. They said that the treatment benefits with CIPA plus miglustat have improved their quality of life. The treatment has also benefited people around them because they are less dependent on others. The committee concluded that CIPA plus miglustat is a valuable additional treatment option that offers potential benefit for people with LOPD and their families.

Treatment pathway

3.4 CIPA plus miglustat is indicated both for people who have had previous ERT treatment and for people who have not had ERT. The clinical expert said that, while most people with LOPD are treated with ALGLU in the NHS, this is expected to change with the availability of AVAL. They explained that the data for CIPA plus miglustat and for AVAL suggested a more durable treatment effect than for ALGLU. So, it was likely that

newly diagnosed people would start on AVAL or CIPA plus miglustat. People currently taking ALGLU would also be switched to AVAL or CIPA plus miglustat when response to ALGLU began to wane. The clinician would look at someone holistically when considering whether to switch treatment. They would take into consideration outcomes on a range of tests assessing muscle and respiratory function. These tests include, but are not limited to, the 6-minute walk test (6MWT), forced vital capacity (FVC) % predicted, time taken to stand from a chair and daily life activities. The clinical expert said there was insufficient data available to determine whether CIPA plus miglustat or AVAL would be preferred as first-line treatment. Given the allergic reactions experienced by some people to ERTs, the possibility of changing to new treatments is also important. They confirmed that CIPA plus miglustat would be considered for:

- people with newly diagnosed Pompe disease
- when the condition has not responded to ALGLU or AVAL
- when ALGLU or AVAL are not tolerated
- people whose condition has worsened clinically after initial response to ALGLU or AVAL.

  The topic of stopping ERT was also discussed. The clinical expert said there are no clinical guidelines on when ERT should be stopped. In their experience, if there is deterioration on current treatment, they would switch to another ERT. They would continue this approach until all ERT options had been tried. If the person's condition continued to decline on the final treatment option at the same rate, for 1 to 2 years, they would consider stopping treatment all together. But, in their experience of stopping treatment for 2 people, rate of decline increased when treatment was stopped. This showed that the treatment had still been providing some benefit. The EAG noted that it would be very challenging to model treatment sequencing and stopping because of a lack of data. The committee concluded that CIPA plus miglustat would be considered for people who had and who have not had ERT.

Comparators

3.5 In the company's original base case, CIPA plus miglustat was compared with ALGLU. A comparison of CIPA plus miglustat against AVAL was only included in scenario analyses. The company said that this was because AVAL was not commercially available in the UK at the time of its submission. Following technical engagement, the company agreed to include AVAL as a comparator in its base case. But it argued that, of the 2 comparators, ALGLU was the most relevant because of its greater use in NHS practice. The clinical expert explained that it was a very fast moving treatment scenario. They expect many people with Pompe disease will be switched to AVAL in the NHS and that it will be used preferentially over ALGLU as a first-line treatment (see section 3.4). The EAG said that both AVAL and ALGLU should be considered as comparators, in line with the NICE scope. The committee concluded that both AVAL and ALGLU were relevant comparators.

Clinical effectiveness

Data sources

3.6 The key clinical evidence for CIPA plus miglustat comes from the PROPEL trial and ATB200-02. PROPEL was a double-blind randomised phase 3 study comparing CIPA plus miglustat (n=85) with ALGLU plus placebo (n=40). The study included people with LOPD who had had ERT for at least 2 years ('ERT experienced') and people who had not had ERT ('ERT naive'). The primary outcome was the 6MWT. Key secondary outcomes included respiratory function, muscle strength, motor function and quality of life. ATB200-02 was a phase 1 and 2 single-arm study that assessed the safety, tolerability, pharmacokinetics and pharmacodynamics of CIPA plus miglustat at different doses. A long-term extension also assessed efficacy. Key data on the comparator treatments came from the COMET and LOTS studies. There was no data that directly compared CIPA plus miglustat with AVAL, so an indirect treatment comparison was used. The committee concluded that the evidence was limited, but acceptable for decision making.

Generalisability

3.7 The clinical expert said that the baseline characteristics for the people in PROPEL and ATB200-02 studies largely reflect the real world population in the NHS. They noted that the trial did not include people at the mildest or most severe ends of the spectrum of LOPD severity. But they advised that treatment is typically only started when people begin to have respiratory or motor decline. So, excluding people with very mild LOPD was consistent with NHS clinical practice. Also, people with very severe LOPD have less capacity to benefit from treatment. In addition, different outcome measures would be used in people with very severe LOPD (for example, you cannot use a 6MWT for people who are unable to walk independently). The company noted that there was a small cohort of people who were unable to walk in ATB200-02 and that they showed improvements in other relevant outcomes (such as upper limb strength). Overall, the clinical expert concluded that most of the people with LOPD that they see were reflected in the baseline characteristics of the CIPA plus miglustat studies. The committee concluded that the data was generalisable to NHS practice.

Treatment effects in the whole population

3.8 In PROPEL, at 52 weeks, people in the CIPA plus miglustat group walked further on average (in the 6MWT) than at baseline compared with people in the ALGLU group (20.8 m compared with 7.2 m). This difference was described as 'clinically meaningful' according to predefined thresholds, but was not statistically significant. FVC% predicted declined in both groups, but the CIPA plus miglustat group showed a slower decline than the ALGLU group (a 0.93% decline compared with a 3.95% decline). This decline was described as 'clinically meaningful' and was statistically significant. The clinical expert said that, although the change in FVC% predicted between the 2 groups was small, it was consistent over time and aligned with results from other studies. They also said that they were not surprised that 6MWT improved in both groups while respiratory function declined in both groups. They noted that the muscles involved in these functions are different and the clinical presentation varies between people (some have more respiratory involvement, some more motor involvement). So, the outcomes would not necessarily change in

parallel. CIPA plus miglustat also showed benefit over ALGLU in patient reported outcome measures. In the Subject's Global Impression of Change scale, more people said they were improving or stable in the CIPA plus miglustat group than in the ALGLU group. The exact results are considered confidential by the company and cannot be reported here. Study ATB200-02 provided longer-term data on the treatment effect of CIPA plus miglustat. It suggested that the treatment effect of CIPA plus miglustat lasts beyond the 12 months assessed in the PROPEL trial, with improvements in 6MWD and FVC% predicted seen 48 months from baseline. The exact results are considered confidential by the company and cannot be reported here. The clinical expert suggested that CIPA plus miglustat may have a more durable response than ALGLU because it may remove glycogen from muscles more efficiently. But, because ATB200-02 was a single-arm study (with no comparator), the committee concluded that there was uncertainty over the long-term benefit of CIPA plus miglustat compared with ALGLU.

Treatment effects in population subgroups

3.9 When the population was considered as 2 prespecified subgroups (ERT experienced and ERT naive), the results were mixed. For the key outcome measures (6MWD and FVC% predicted), the response in the ERT-naive subgroup appeared to be slightly better with ALGLU than with CIPA plus miglustat. But there were only 7 people in the ALGLU group of the ERT-naive subgroup, so the results were highly uncertain. But response in the ERT-experienced subgroup, who had had ERT for an average of 7.4 years before the study began, was better with CIPA plus miglustat than with ALGLU. The plausibility of LOPD not treated with ERT having a different response to LOPD treated with ERT was discussed. The clinical expert explained that people who have not had ERT may have more potential to benefit from treatment than people who have had it. This is because, having not had ERT, their muscles will have built up a lot of glycogen that needs to be removed. Their muscles are also likely to be in a healthier state because they are probably younger and have had the condition for less time. People who have had ERT may have less potential for benefit because a lot of the excess glycogen will already have been removed from their muscles. Also, they may already have less muscle mass because of being older than people who have never had

ERT or because of having had LOPD for longer. So, the clinical expert said they would expect a more modest treatment effect in the ERT-experienced subgroup. The committee noted that people who have had ERT would already have benefited from their initial 'boost' of ERT treatment with ALGLU and may have been in the treatment-effect waning stage. So, it may be expected that the CIPA plus miglustat group would have shown a greater improvement because of not having had ERT. The company said that the subgroup analysis from PROPEL showed this pattern. It explained that both of the ERT-naive subgroups showed a benefit from treatment, but the ERT-experienced subgroup in the ALGLU group showed little response. The committee concluded that it is plausible that ERT treatment effects are different in people who have not had ERT compared with people who have had ERT.

Indirect treatment comparison

3.10 Because there is no direct evidence comparing CIPA plus miglustat with AVAL, the company did an indirect treatment comparison. The company used a multilevel network meta-regression (ML-NMR) to estimate the treatment effects in a mixed population (ERT naive and ERT experienced). In the company's original base case, 7 studies were used in the network, but 2 single-arm studies were removed during technical engagement. So, the company's updated base case was based on 5 randomised controlled studies:

- PROPEL (CIPA plus miglustat compared with ALGLU)
- LOTS (ALGLU compared with placebo)
- LOTS open-label extension (ALGLU)
- COMET (AVAL compared with ALGLU)
- COMET open-label extension (AVAL).

Baseline characteristics were adjusted for using individual patient data from PROPEL (age, gender, ethnicity, previous ERT duration, baseline 6MWD and FVC% predicted). ERT duration was included as a continuous covariate in the regression (the number of months on treatment). The EAG said that including it

as a binary covariate (that people either have had or not had previous treatment, rather than the number of months on treatment) may have been more appropriate. This was because having or not having previous ERT treatment was a more influential factor than duration of that treatment. The results confirmed that CIPA plus miglustat seemed more effective compared with ALGLU both for 6MWD and for FVC% predicted. But the results for all other comparisons had wide confidence intervals and the conclusions were uncertain. The committee concluded that it was difficult to draw firm conclusions about the relative long-term treatment effect of CIPA plus miglustat compared with AVAL. This was because of the different patient populations included in the studies and small sample sizes. But, given the rarity of the condition, the scarcity of robust data is unlikely to be resolved. So, the committee was willing to assume that CIPA plus miglustat had similar efficacy to that of AVAL.

Economic model

Company's modelling approach

3.11 The company used a state transition patient-level simulation model with 7 living health states (plus death). The health states were associated with different costs, quality of life and mortality risks. People entered into the model needing no respiratory or mobility support, and then moved through the health states as LOPD progressed. The committee was concerned that the model did not reflect likely future NHS practice, when people would switch to a different ERT when they began to deteriorate on their existing treatment (see section 3.4). But it acknowledged that there was a lack of robust data to enable ERT treatment sequencing to be modelled. The committee concluded that, although there were limitations with the modelling approach, it was unlikely that these could be overcome. So, it considered the results of the cost-effectiveness model alongside the total annual treatment costs and results of the indirect treatment comparison.

Subgroups

3.12 The company's preferred approach was for the cost effectiveness of

CIPA plus miglustat to be considered in the whole population, rather than in separate subgroups (ERT naive and ERT experienced). It explained that it considered the whole population (based on PROPEL, in which 77% of people had had ERT) to better reflect the real world, in which most people with LOPD have had ERT. The EAG said that, because there may be a different treatment effect in the 2 subpopulations (see section 3.9), the cost effectiveness of the intervention should have been considered in the separate subgroups. It also noted that there were other differences between the groups, such as baseline characteristics and health states. Given the very small number of people who had not had ERT in PROPEL, the EAG said that it was difficult to draw any firm conclusions about the clinical or cost effectiveness of CIPA plus miglustat in this group. The EAG said that, by considering the groups separately, it was easier to explore this uncertainty. The committee concluded that it would consider the ERT-naive and ERT-experienced groups separately.

Model inputs

Efficacy data

3.13 The efficacy inputs used in the model came from a range of sources.

- ALGLU: ML-NMR data was used to model efficacy from baseline to year 1. ALGLU efficacy from year 1 onwards was based on published data from a Pompe patient registry.
- CIPA plus miglustat: PROPEL data was used to inform the efficacy from baseline to year 1. A hazard ratio for CIPA plus miglustat relative to ALGLU was estimated from year 1 onwards.
- AVAL: ML-NMR data was used to model efficacy from baseline to year 1. A hazard ratio relative to ALGLU was estimated from year 1 onwards.

  Because of the lack of long-term comparative data, there was considerable uncertainty in the hazard ratios used to compare CIPA plus miglustat with ALGLU, and AVAL with ALGLU. The exact hazard ratios used in the company's base case are considered confidential by the company and cannot be reported

here. The company cited clinical expert opinion that suggested there will be LOPD progression in people having CIPA plus miglustat in the long term because the treatment is not curative. But the rate of decline is expected to be slightly lower, with a delayed waning effect, compared with ALGLU. The EAG explored a number of different hazard ratios in scenario analyses. The clinical expert said that a hazard ratio of 0.85 for CIPA plus miglustat compared with ALGLU was reasonable. It would mean that, in people on CIPA plus miglustat, LOPD would progress 15% more slowly than in people on ALGLU (see section 3.8). But the clinical expert noted that this estimate was uncertain because the long-term data was not available to substantiate it. The clinical expert also noted that it was unclear whether AVAL and CIPA plus miglustat would have the same benefit in comparison with ALGLU. The pivotal trial for AVAL only included people who had not had ERT, while the PROPEL trial for CIPA plus miglustat mainly included people who had had ERT. This meant it was not possible to make a robust comparison of CIPA plus miglustat and AVAL. The committee agreed that the hazard ratios for CIPA plus miglustat compared with ALGLU and AVAL compared with ALGLU were highly uncertain. It concluded that it was reasonable to assume that both CIPA plus miglustat and AVAL slow down LOPD progression compared with ALGLU. It also concluded that it was reasonable to assume that both CIPA plus miglustat and AVAL have similar efficacy (see section 3.10), but that there was considerable uncertainty in this assumption. So, its preference was to apply a hazard ratio of 0.85 to CIPA plus miglustat compared with ALGLU and to AVAL compared with ALGLU.

Utility values

3.14 Utility values for the model came from the PROPEL study. But they were supplemented by vignette values because PROPEL could not be used to inform the utility values for 'later' health states (needing invasive respiratory support or a combination of mobility and respiratory support). This was because most people in the study had not yet reached those health states in the follow-up period. The vignettes were developed using clinical trial data and a targeted literature review. They were refined and validated using interviews with 12 adults with LOPD and 2 clinicians specialising in LOPD. The EAG noted that the vignette study appeared to generate lower utility values than those for the equivalent group in the PROPEL study (in which both sets of data were available). The

committee concluded that, although there was some uncertainty remaining in the utility values, they were suitable for decision making.

Resource use

3.15 Resource use was estimated from clinical opinion and was aligned with NICE's technology appraisal guidance on avalglucosidase alfa when possible. The EAG was concerned that the costs used in the company model for invasive home mechanical ventilation may have overestimated the cost of invasive ventilation. They came from a paediatric population (sourced from Noyes et al. 2006), which the EAG said may have limited their generalisability to an adult population. The company referred to clinical opinion, which suggested that Noyes et al. was likely to have substantially underestimated these costs, and that costs would not vary substantially between adult and paediatric populations. Clinical expert opinion also suggested that most people needing respiratory support can have non-invasive ventilation. The EAG noted that invasive ventilation costs were a model driver for the comparison of CIPA plus miglustat with ALGLU, and suggested that a conservative approach may be appropriate. The committee acknowledged the uncertainty around this parameter. It considered scenarios using both the Noyes et al. data and data from Gajdos et al. (2021), a study identified by the EAG which was conducted in Czechia. The committee noted that, regardless of which scenario was used, the most cost-effective treatment option remained the same.

Cost-effectiveness estimates

Net health benefit available

3.16 Cost effectiveness was assessed by calculating net health benefit. This was because, in some scenarios, CIPA plus miglustat had lower total costs and lower total quality-adjusted life years (QALYs) than one of the comparators. Net health benefit can be a more useful and informative figure than incremental cost-effectiveness ratios in this case. The net health benefit of CIPA plus miglustat was compared with that of AVAL and of ALGLU using pairwise comparisons, at threshold values of

£20,000 per QALY gained. The incremental benefit of CIPA over AVAL and AVAL over ALGLU was considered by comparing the size of the net health benefit for each comparison. The committee noted that there was considerable uncertainty around the long-term benefit of CIPA plus miglustat compared with ALGLU. There was also uncertainty around the treatment effect of CIPA plus miglustat compared with AVAL. This was because of the absence of direct comparative data and the differences in the patient populations in the clinical trials. The committee explored the effect of this uncertainty through a range of scenarios that used different hazard ratios for the treatment effects. It also considered the company's probabilistic sensitivity analysis, although probabilistic results including the confidential commercial arrangements were not available because of excessive computational burden. But the committee considered that it was unlikely that this uncertainty could be resolved using any currently available data, or any which is planned to be collected in the near future. The committee also had concerns about the structure of the model. This was because it did not sequence treatments, which would have reflected the likely pathway of someone in the NHS who would switch ERT when their condition began to deteriorate on current treatment. But again, it thought that this uncertainty could not be resolved because the treatment pathway was changing and there was insufficient data. Taking this into account, the committee considered the net health benefits for its preferred hazard ratios in the 2 separate subpopulations (ERT naive and ERT experienced). Because of uncertainty around the modelling approach, it also considered the total annual costs of the treatment options alongside the assumption of similar efficacy between CIPA plus miglustat and AVAL (see section 3.10). With these assumptions, there was a positive incremental net health benefit for CIPA plus miglustat compared with both AVAL and ALGLU in both subpopulations. (Because of confidential commercial arrangements for the intervention and comparator treatments in the pathway, the exact net health benefits cannot be reported here.) The committee concluded that the results confirmed that CIPA plus miglustat was cost effective compared with AVAL and with ALGLU at £20,000 per QALY gained for the ERT-naive and ERT-experienced populations.

Other factors

Equality issues

3.17 The committee concluded that the recommendations would not have a different effect on people protected by equality legislation than on the wider population.

Severity

3.18 The QALY shortfall calculated for LOPD did not meet the threshold for the severity modified to be applied.

Conclusion

Recommendation

3.19 The clinical data for CIPA plus miglustat showed improvements in LOPD in adults compared with ALGLU. There is uncertainty around the long-term benefit compared with ALGLU, and also around the comparison with AVAL. But, even accounting for this uncertainty, the cost-effectiveness estimates for CIPA plus miglustat showed a positive net health benefit compared with both AVAL and ALGLU. So, CIPA plus miglustat is recommended as an option for treating LOPD in adults, at first line and later lines of therapy.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication. Because cipaglucosidase alfa plus miglustat has been available through the early access to medicines scheme, NHS England and integrated care boards have agreed to provide funding to implement this guidance 30 days after publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has late-onset Pompe disease and the doctor responsible for their care thinks that cipaglucosidase alfa plus miglustat is the right treatment, it should be available for use, in line with NICE's recommendations.

4.4 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE highly specialised technologies guidance. When a NICE highly specialised technologies guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

James Fotheringham
Vice Chair, technology appraisal committee A

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Alex Sampson, Madiha Adam
Technical leads

Jo Richardson
Technical adviser

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ISBN: 978-1-4731-5290-8