Multi-stakeholder engagement leading to access to treatment for MPS IVA (Morquio A) – a model for the ultra-rare disease community(BM)

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Objectives

To achieve reimbursement for elosulfase alfa for MPS IVA patients resident in England.

Background

- MPS IVA is an ultra-rare disease affecting less than 100 patients in England.
- In 2013, responsibility for the reimbursement decision making process for treatments for rare diseases, formerly governed by the Advisory Group for National Specialised Services, was replaced by a joint process involving the Highly Specialised Technologies Evaluation Committee of NICE and the Programme of Care Group of NHS England.
- The only treatment currently available, elosulfase alfa, was licensed by the European Medicines Agency on 28th April 2014.
- The UK had been a major contributor to the Phase III clinical trial with 35 patients being enrolled out of the 176 recruited worldwide.
- Interim funding was not available when elosulfase alfa was licensed and there was a high degree of interest and concern in continuing access to treatment in England.
- Although patients who had taken part in the clinical trial continued to receive free drug, other English MPS IVA sufferers had no access to treatment.

Methods

On the 21st November 2014, a 10 year old boy, supported by the MPS Society legally challenged NHS England's scorecard decision method. This marked the start of a year long process involving the engagement of all stakeholders to develop a workable solution for treatment access (Figure 1). Patients together with the patient organisation MPS Society UK, members of Parliament and clinicians canvassed NHS England and the Department of Health for a fair process with equal access to therapies as for common disorders (Figure 2).

This resulted in elosulfase alfa for MPS IVA being referred to NICE for full evidence review and decision. During the NICE process, the MPS Society suggested a robust procedure whereby all patients that met a set of criteria would be able to access treatment (Figure 3). Stopping criteria were also included for the first time ever. This was incorporated by NICE and announced in their draft guidance in September 2015.

The development of the Managed Access Agreement (MAA) became a working partnership between NHS England, NICE, the MPS Society, BioMarin and a clinical expert.

The MAA was designed to be inclusive for patients, ensuring response to treatment in a minimum of 4 out of 5 criteria through consistent clinical and quality of life monitoring. An intensive follow up programme and multi domain assessments would be required and treatment would stop for those not meeting treatment targets (Table 1).

Results

On 16th December 2015 NICE guidance recommended elosulfase alfa for patients in England via the MAA.[1,2] As of 31st May 2016, a total of 46 patients have been recruited to the MAA through 7 hospitals in England. This represents 48% of the 95 patients known to have MPS IVA in England. Of these, 27 patients previously took part in the clinical trials for elosulfase alfa, and 19 patients are receiving this new treatment for the first time.

Table 1. Response criteria for continued treatment[4]

Response criteria	Naïve patient (in 1st year of treatment)	Previously treated patients (2nd year or more on treatment)
Improvement of 6 MWT or 25ft Ambulation Test	10% Improvement over baseline	Remains 5% above baseline
Improvement in FVC or FEV-1	5% Improvement over baseline	Remains 2% above baseline
Stabilisation defined as no adverse change in the numerical value in two of the following three measures: • Quality of Life as measured by the EQ5D-5L or MPS HAQ Caregiver Domain • Beck depression inventory • Adolescent Paediatric Pain Tool or Brief Pain Inventory depending on age	Stabilisation	Stabilisation
Reduction in urinary keratan sulfate	20% Reduction from baseline	Remain reduced at least 20% from baseline value
Decline in ejection fraction as measured by echocardiogram	Decline of less than 10% from baseline	Decline of less than 10% from baseline

FEV: forced expiratory volume, FVC: forced vital capacity, MWT: minute walk test

Figure 3. The Managed Access Agreement criteria[2]

Start criteria

- Confirmed diagnosis of MPS IVA
- Confirmed enzymatic test, elevated urinary keratan sulfate and mutation analysis
- Sign up to the 'Managed Access Patient Agreement'
- Full set of baseline assessments obtained for patients over 5 years of age

Exclusion criteria

- Patient is diagnosed with an additional progressive life limiting condition where treatment would not provide long term benefit e.g. cancer or multiple sclerosis
- Patient has a lung capacity (FVC) of less than 0.3 litres and requires ventilator assistance
- Patient is unwilling to comply with the associated monitoring criteria

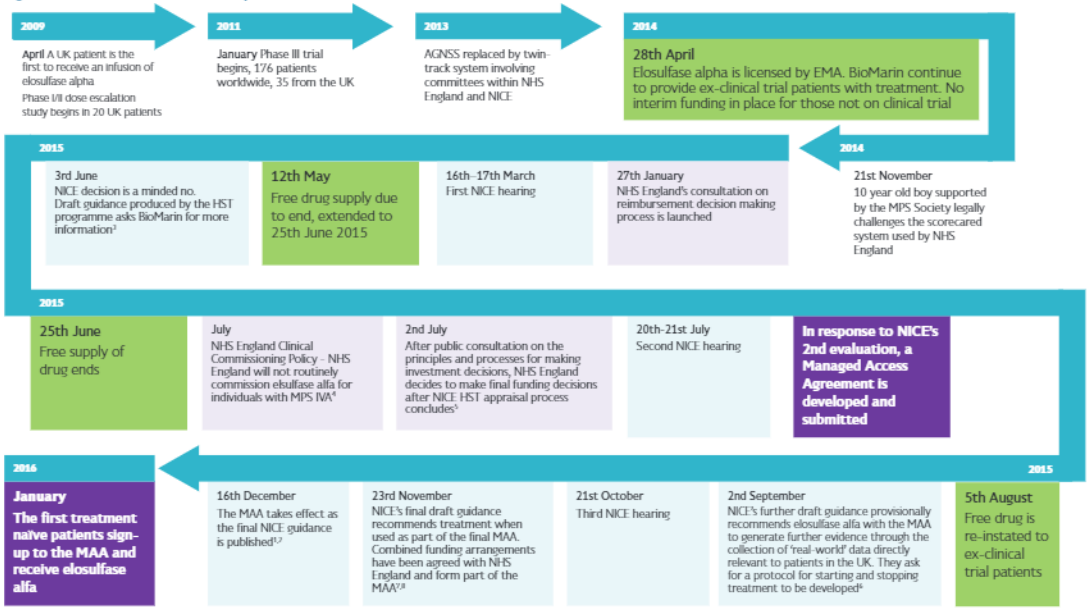
Stop criteria

- Non-compliance with assessments for continued therapy (non-compliance is defined as fewer than three attendances for assessment in any 14 month period)
- Patient fails to meet 4 of the 5 treatment response criteria (Table 1)
- Patient is unable to tolerate infusions due to infusion related severe adverse events that cannot be resolved

Patients who are taken off treatment will continue to be monitored for disease deterioration and supported with other clinical measures.

FVC: forced vital capacity.

Figure 1. The reimbursement decision process



AGNSS: Advisory Group for National Specialised Services; EMA: European Medicines Agency; HST: Highly Specialised Technologies

Figure 2. MPS IVA patients, families, the MPS Society and MPs, campaign for treatment access

- Engagement with 40 MPs, parliamentary questions led by Greg Mulholland, MP
- 3 meetings with the Minister for Life Sciences George Freeman
- 2 Adjournment Debates
- MPS Society hosted Westminster Hall event attended by MPs and peers, pharma representatives, patient organisations and the BBC
- 6 protests
- Parent met with the Prime Minister David Cameron
- Online petitions 'NHS England's scorecard system denies access to treatment for ultra-rare diseases' and 'Call for interim funding'
- Articles in the national and local press
- Social media campaign #fundourdrugsNOW #fight4treatment

Clockwise from left: Kamal (left) and Sam outside 10 Downing Street; Luke (left) and Olivia campaigning; Sunday Express cover story from 12 July 2015; and Kamal (left) and Sam campaigning with MPs, parents and members of MPS Society.

> "There have been a couple of signs of Vimizim doing something…I have been in the garden for the first time in a long time last week and for the first time ever, I saw the legs of a caterpillar!! This may seem daft and simple, but due to the clouding of my corneas I have never seen much detail on anything.
>
> A patient's experience of treatment

Conclusions

In an environment where health systems are having to choose between high cost drugs and the funding of other health resources, the MAA, with a confidential financial arrangement, offers all patients meeting the treatment criteria access to reimbursed therapy in the first 12 months. The MAA will be subject to annual review under the chairmanship of NICE and the data collected will be used to assess whether NICE will continue to fund the treatment after the 5 year term of the MAA.

Whilst we are in the first year of this new initiative, MPS IVA patients have embraced the MAA and recognised that adherence to the MAA is the only way forward to ensure continued access to treatment. Only time will tell if the stopping criteria are fair and if patients affected by common disorders will become subject to similar requirements in the future to ensure equity across all aspects of health.

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