Chair's presentation

Strimvelis for the treatment of adenosine deaminase deficiency-severe combined immunodeficiency

2nd Evaluation Committee meeting

Highly Specialised Technologies committee, 23 November 2017

Lead team: Jeremy Manuel, Sarah Davis, Vincent Kirkbride

Company: GlaxoSmithKline

Chair: Peter Jackson

Evidence review group: York Technology Assessment Group

NICE team: Thomas Strong, Ian Watson, Sheela Upadhyaya

Strimvelis
GlaxoSmithKline

Marketing authorisation	Indicated for treating severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), for whom no suitable human leukocyte antigen (HLA)- matched related stem cell donor is available
Mechanism of action	Gene therapy containing autologous $CD34^+$ cells transduced *ex vivo* with a replication-deficient retroviral vector containing the correct form of the human ADA gene in the DNA sequence
Administration & dose	• Must be administered in a specialist transplant centre at HSR-TIGET, Milan, Italy • 5 million purified CD34+ cells/kg required per patient; recommended that patients have pre-treatment with busulfan • Single intravenous infusion
List price	Manufacture of Strimvelis = €594,000

Source: Strimvelis summary of product characteristics; Company submission

ECD preliminary recommendation

Strimvelis was recommended as an option for treating ADA–SCID when no HLA-matched related stem cell donor is available

- Committee noted ADA–SCID is a devastating condition that begins in infancy, which impacts all aspects of life for patients, families and carers
- Strimvelis is effective in treating ADA–SCID, but the comparative evidence for hematopoietic stem cell transplant was very limited
- Key drivers within the model were uncertain, and many additional benefits were not captured and had to be considered qualitatively
- With additional QALY weighting, the plausible ICER estimates are lower than the level normally considered acceptable for HST
- Strimvelis is likely to provide important benefits for people with ADA–SCID, at a cost that provides value for money in HST

ECD consultation responses

- Consultee comments from:
  - GSK
  - Primary Immunodeficiency UK
  - NHS England
- Clinical and patient experts:
  - None
- Commentator comments from:
  - Welsh Health Specialised Services Committee
- Web comments from:
  - None
- No comment response from Department of Health and Genetic Alliance UK

ECD consultation comments
Primary immunodeficiency UK

- Welcomes the positive recommendation
- Would welcome details on implementation in England and Wales, and funding for travel and accommodation
- Due to risk of oncogenic events, long-term follow up is essential
  - NICE guidance should give details of what requirements need to be met and who is responsible
- Welcomes that evidence from patients and benefits in addition to direct health benefits have been taken into account in committee's decision-making

⊙ ***Are there any long-term follow up requirements to take into account?***

ECD consultation comments
NHS England

- Confirm a travel and accommodation policy, building on experience of proton beam therapy, will be developed
- Previously been suggested that additional procedures or extended hospitalisation in Italy should be funded through the 'S2' route, where people would incur additional charges equal to Italian statutory patients
  - NHSE do not have access to the 'S2' route, as held by Department of Health
  - NHSE expect to contract directly with the hospital in Milan and pay charges equal to Italian statutory patients, but this has not yet been agreed
  - This would assure NHSE that patients receive the same quality service as they would in England.
- Confirms that arrangements can be implemented within the standard timelines

⊙ ***Are there any implementation issues to take into account?***

ECD consultation comments
Welsh Health Specialised Services Committee

- WHSSC has contacted NHS England to suggest a collaboration to develop a common referral pathway, protocol and commissioning policy
  - May also include agreeing suitable gate-keeping arrangements
  - Collaboration agreed in principle and further discussion planned for early in 2018
  - Anticipate funding of travel and accommodation for people in Wales having Strimvelis and their families will be assessed using similar model to that already in use for Proton Beam Therapy
- WHSSC will be writing to the Welsh Government Minister requesting an extension to standard implementation timelines in Wales (60 days)
  - Due to scale of service planning required for this treatment
  - Expecting to complete from April 2018 (the standard implementation timelines in England)

⊙ ***Are there any implementation issues to take into account?***

ECD consultation comments
GSK (I)

- Welcomes the positive recommendation
- Provided comment on several of the committee's preferred assumptions

Committee rationale at ECM1	GSK comment
PEG-ADA duration	
• Preferred assumption that PEG-ADA duration equal across treatments – people would remain on PEG-ADA if their condition was unstable, and durations observed in the Strimvelis trial were longer than the model	• GSK accepts there is uncertainty, but still believes there is justification for shorter PEG-ADA duration for Strimvelis – as there is no search for a donor
Rescue HSCT	
• Considered it most likely that people would receive rescue therapy from a matched unrelated donor. • Evidence on rescue rates was very limited and it was plausible rescue rates across treatments would be equal	• GSK accepts that matched unrelated donor may be more common, but notes that if matched sibling donor available this would be the 1st choice • If rates of rescue transplant were equal this would also increase the QALY weighting that could apply for Strimvelis

ECD consultation comments
GSK (II)

Committee rationale at ECM1	GSK comment
Long-term utilities	
• Considered implausible that utilities were equal to the general population after year 8 – restoration to a lower utility should be used • Specific utilities uncertain, but preferred ERG's approach (disutilities for congenital hearing loss) because it was based on available evidence	• GSK notes the 20% long-term utility reduction in its sensitivity analysis is intended only to test extreme values • Agrees there is some long-term morbidity, but ERG overestimates the decrement • Patient experts stated that long-term impairment does not prevent people from living a near-normal life
Discount rate	
• Committee considered both the 1.5% and 3.5% discount rates, as it was highly uncertain whether Strimvelis would lead to 'normal or near-normal health'	• GSK notes 1.5% discount rate is commonly used where benefit accrues long after intervention, e.g. public health programmes • NICE previously accepted a 1.5% discount for HST1 and TA235

⊙ ***Any changes in committee's preferred assumptions from ECM1?***

Key issues for consideration

- Any changes in committee's preferred assumptions from ECM1?
- Are there any implementation issues to take into account?
- Are there any long-term follow up requirements to take into account?
- Has the committee heard anything in consultation to change its preliminary recommendation?