NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Strimvelis for treating severe combined immunodeficiency caused by adenosine deaminase deficiency

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of Strimvelis within its licensed indication for treating severe combined immunodeficiency caused by adenosine deaminase deficiency for national commissioning by NHS England.

Background

Immunodeficiency is caused by failure of a component of the immune system and results in increased susceptibility to infections. Severe combined immunodeficiency caused by adenosine deaminase deficiency (ADA-SCID) is a disease in which the body cannot make functional lymphocytes (a type of white blood cell) and, as a result, patients have a severely impaired immune system. A faulty gene inherited from both parents impairs production of an essential protein called adenosine deaminase, which is particularly important for the formation of lymphocytes and a functioning immune system. This deficiency usually results in the onset of serious infections within the first few months of life. The symptoms of ADA-SCID include an increased susceptibility to infections and failure to thrive; ADA-SCID also has non-immunological manifestations, including neurological and developmental effects. ADA-SCID is chronically debilitating and life-threatening.

ADA-SCID accounts for about 10–15% of all diagnoses of severe combined immunodeficiency[1]. The overall annual incidence is estimated to be between 1 in 200,000 and 1 in 1,000,000 live births[1], although the incidence varies widely between populations; it is estimated that approximately 10 people are born with ADA-SCID per year in England.

Diagnosis of ADA-SCID includes lymphocyte count, immunoglobulin testing and biochemical and genetic testing. Initial management includes treatment with antibiotics, antiviral and antifungal medicines, intravenous immunoglobulins and prophylaxis for *Pneumocystis jiroveci* (a type of fungal pneumonia), but most people with ADA-SCID ultimately require a bone marrow transplant. Treatment is based on allogeneic haematological stem cell transplantation (HSCT), ideally from a human leukocyte antigen (HLA)-matched related stem-cell donor. However, for about half of people with ADA-SCID, an HLA-matched related donor cannot be found, and other treatment options include HSCT from an HLA-matched unrelated donor, an HLA haploidentical donor (usually a parent) or umbilical cord derived stem cells. Enzyme replacement therapy with pegylated adenosine deaminase enzyme (does not currently have a marketing authorisation in the UK) is often

considered in clinical practice as a short-term option before a bone marrow transplant.

The technology

Strimvelis (GlaxoSmithKline) is a 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. The patient's haematopoietic progenitor and stem cells are harvested from the bone marrow and purified. These are then modified using a viral vector to insert one or more copies of the ADA gene into the cells. When sufficient transduced cells are produced, the patient has pre-treatment with busulfan and the transduced cells are reintroduced into the patient.

Strimvelis has a marketing authorisation for treating severe combined immunodeficiency caused by adenosine deaminase deficiency (ADA-SCID), in people for whom no suitable human leukocyte antigen (HLA)-matched related stem cell donor is available.

Intervention(s)	Strimvelis (retroviral-transduced autologous $CD34^+$ cells)
Population(s)	People with ADA-SCID for whom no suitable HLA-matched related stem cell donor is available
Comparators	Bone marrow transplant (including HSCT from an HLA-matched unrelated donor or HSCT from an HLA-haploidentical donor)
Outcomes	The outcome measures to be considered include: • overall survival • intervention-free survival • immune function (including rate of severe infection, lymphocyte counts, thymopoiesis, use of intravenous immunoglobulin, vaccination response) • non-immunological aspects of ADA-SCID (including neurological and developmental effects) • need for and duration of in-patient treatment • adverse effects of treatment • health-related quality of life (for patients and carers).
Nature of the condition	• disease morbidity and patient clinical disability

	with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options
Clinical Effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• Cost effectiveness using incremental cost per quality-adjusted life year • Patient access schemes and other commercial agreements • The nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.

Other considerations	If the evidence allows, subgroups based on the degree of HLA matching for HSCT (that is, people for whom matched unrelated or haploidentical HSCT is available) will be considered. The analysis will include consideration of the duration of enzyme replacement therapy with pegylated adenosine deaminase in people treated with the intervention or comparator, and should include any relevant differences in costs or outcomes associated with this. Guidance will only be issued in accordance with the marketing authorisation Guidance will take into account any Managed Access Arrangements
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2016) Manual for prescribed specialised services 2016/17. Chapter 100: Severe combined immunodeficiency and related disorders service (children) NHS England (2013) NHS standard contract for severe immunodeficiency and related disorders service (children) Department of Health (2014) NHS Outcomes Framework 2015-2016. Domains 1, 2, 4 and 5.

References

1. Orphanet (2012) Severe combined immunodeficiency due to adenosine deaminase deficiency. Accessed April 2017.