NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

GSK2696273 for treating severe combined immunodeficiency caused by adenosine deaminase deficiency

Draft scope (pre-referral)

Draft remit/evaluation objective

To evaluate the benefits and costs of GSK2696273 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 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 stops 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, failure to thrive and weight gain. ADA-SCID is chronically debilitating and life-threatening.

ADA-SCID accounts for about 10–15% of all diagnoses of severe combined immunodeficiency.[1] The annual incidence is estimated to be between 1 in 200,000 and 1 in 1,000,000 live births, which is equivalent to approximately 1 to 3 people born in England with the condition.[1,2] ADA-SCID affects men and women equally.

Diagnosis of SCID includes lymphocyte count and immunoglobulin testing (lgG, A and M). Initial management of ADA-SCID includes treatment with antibiotics, antiviral and antifungal medicines, intravenous immunoglobulins and prophylaxis for *Pneumocystis jiroveci* (a type of fungal pneumonia), but most ultimately require a bone marrow transplant. Treatment is based on allogeneic haematological stem cell transplantation (HSCT) from a human leukocyte antigen (HLA)-matched related stem cell donor. However, most people lack a matched related donor 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, or enzyme replacement therapy with pegylated adenosine deaminase enzyme (which does not currently have a marketing authorisation in the UK for any indication).

The technology

GSK2696273 (brand name unknown, 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, they are then reintroduced into the patient.

GSK2696273 does not currently have a marketing authorisation in the UK for treating severe combined immunodeficiency caused by adenosine deaminase deficiency. It is being studied in clinical trials in people with SCID-ADA for whom no suitable HLA-matched related stem cell donor is available following pre-treatment with busulfan.

Intervention(s)	GSK2696273 following pre-treatment with busulfan
Population(s)	People with SCID-ADA for whom no suitable HLA-matched related stem cell donor
Comparators	Established clinical management without GSK2696273 (including HSCT from an HLA-matched unrelated donor, HSCT from an HLA haploidentical donor and enzyme replacement therapy with pegylated adenosine deaminase enzyme)
Outcomes	The outcome measures to be considered include: • overall survival • intervention-free survival • rate of severe infection • lymphocyte counts • 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
Impact of the new technology	• clinical effectiveness of the technology • 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)
Cost to the NHS and Personal Social Services (PSS), and Value for Money	• budget impact in the NHS and PSS, including patient access agreements (if applicable) • robustness of costing and budget impact information • technical efficiency (the incremental benefit of the new technology compared to current treatment) • productive efficiency (the nature and extent of the other resources needed to enable the new technology to be used) • allocative efficiency (the impact of the new technology on the budget available for specialised commissioning)
Impact of the technology beyond direct health benefits, and on the delivery of the specialised services	• 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 • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	If the evidence allows, subgroups based on previous treatment with enzyme replacement therapy with pegylated adenosine deaminase enzyme will be considered. Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2014) Manual for prescribed specialised services 2013/14 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.

Questions for consultation

Have all relevant comparators for GSK2696273 been included in the scope? Which treatments are considered to be established practice for treating severe combined immunodeficiency caused by adenosine deaminase deficiency? Is enzyme replacement therapy with pegylated adenosine deaminase enzyme an appropriate comparator for GSK2696273?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

Please describe any existing services in England for the diagnosis and management of this condition.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which GSK2696273 will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Highly Specialised Technologies Evaluation Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might

improve the way that current need is met (is this a 'step-change' in the management of the condition)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: http://www.nice.org.uk/media/DE4/9A/HSTCombinedInterimProcessMethods.pdf.

References

1 Orphanet (2012) Severe combined immunodeficiency due to adenosine deaminase deficiency. Accessed October 2015

2 Office for National Statistics (2015) Birth Summary Tables, England and Wales, 2014. Accessed October 2015