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Press office

Press release

New gene therapy for the treatment of children with ultra-rare immune disorder recommended for approval

Orphan-designated Strimvelis to offer treatment option for patients with ADA-SCID who have no suitable stem cell donor

The European Medicines Agency (EMA) has recommended granting a marketing authorisation in the European Union (EU) for a new gene therapy for the treatment of patients with adenosine-deaminase-deficient severe combined immunodeficiency (ADA-SCID), who have no matching donor for a stem cell transplant. Children born with this disorder have virtually no immunity to fight off everyday bacterial, fungal or viral infections.

ADA-SCID is an ultra-rare immune disorder, caused by a faulty gene inherited from both parents that stops the production of adenosine deaminase. Without this enzyme, the body is unable to break down a toxic substance called deoxyadenosine. The toxin builds up and destroys infection-fighting lymphocytes. Children born with ADA-SCID are severely impaired in their ability to fight infections. The disorder can also lead to various non-immunological health problems, including a failure to grow and develop normally, hearing loss and liver and kidney problems.

Symptoms normally appear in the first six months of life. The disease is usually fatal in the first two years of life, unless the function of the immune system can be restored.

There is no authorised medicine to treat ADA-SCID in the EU. Transplantations of blood-forming stem cells from the bone marrow of a healthy person have been conducted, but the success of this treatment depends on how close is the match between the stem-cell donor and the patient. Typically, ADA-SCID sufferers who receive stem cell transplants from genetically-matched siblings have a good chance of survival and recovery of the immune system. However, survival of patients who have no related matched donor is poor, mainly because of the risk of graft versus host disease, whereby the T-cells in the donated tissue attack the body cells of the recipient. This requires immunosuppressant treatment and increases the risk of infection, the main cause of death after transplantation.

Some patients received enzyme replacement therapy with pegylated adenosine deaminase (PEG-ADA) on a compassionate use basis, although this treatment is not authorised anywhere in the EU. Enzyme replacement requires lifelong weekly injections. Based on the experience so far, there appears to be a



loss in immune function over time in patients receiving PEG-ADA, making them again more susceptible to infections.

Gene therapy could offer an alternative treatment with better prognosis for patients without a suitable transplant donor. Strimvelis is manufactured from a patient's own immature bone marrow cells (called CD34+ cells) into which a normal adenosine deaminase enzyme gene has been inserted. After these cells are injected back into the patient, the cells are able to develop into the different types of blood and immune cells. This is expected to give the patient life-long ability to produce lymphocytes that can fight off infections.

Using a patient's own cells avoids the risk of graft versus host disease, and lowers the risk of infections due to immunosuppression. It also reduces the dose of chemotherapy needed to prepare a patient for treatment compared to bone marrow transplant. Furthermore, gene therapy is not dependent upon a donor search, so it can be made available to any patient.

The effects of Strimvelis were studied in a pivotal clinical trial involving 12 patients. All of the patients included in this trial are still alive, with an average follow-up period of 7 years. The most common side effects observed in this study include pyrexia (fever), increased hepatic enzyme levels, autoimmune reactions, such as anaemia, neutropenia, and autoimmune haemolytic anaemia, aplastic anaemia and thrombocytopenia. This study was carried out in accordance with a Paediatric Investigation Plan (PIP), which was agreed by the Agency's Paediatric Committee. To ensure close long-term follow-up, the applicant for Strimvelis, is required to enrol all patients who receive the medicines, in a registry to monitor and report its long-term effects.

The assessment of Strimvelis was carried out by the Committee on Advanced Therapies (CAT), EMA's specialised scientific committee for advanced therapy medicinal products, such as gene or cell therapies. At its March 2016 meeting, the CAT recommended the adoption of a marketing authorisation for Strimvelis. The CAT's recommendation was considered by the Committee for Medicinal Products for Human Use (CHMP) which agreed with the CAT and issued a positive opinion.

Strimvelis was designated as an orphan medicinal product in 2005. Orphan designation gives medicine developers access to incentives such as fee reductions for scientific advice, or the possibility to obtain 10 years' market exclusivity for an authorised orphan-designated medicine. It is a key instrument available in the EU to encourage the development of medicines for patients with rare diseases.

The applicant received scientific advice from the Agency on various aspects of the application dossier throughout the medicine's development.

The opinion adopted by the CHMP at its March 2016 meeting is an intermediary step on Strimvelis' path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role/use of this medicine in the context of the national health system of that country.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. The applicant for Strimvelis is GlaxoSmithKline Trading Services.
3. Following this positive CHMP opinion, the COMP will assess whether the orphan designation should be maintained.
4. More information on the work of the European Medicines Agency can be found on its website:
www.ema.europa.eu

Contact our press officers

Monika Benstetter

Tel. +44 (0)20 3660 8427

E-mail: press@ema.europa.eu

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