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Press release

New gene therapy to treat spinal muscular atrophy

EMA has recommended granting a conditional marketing authorisation in the European Union for the gene therapy Zolgensma (onasemnogene abeparvovec) to treat babies and young children with spinal muscular atrophy (SMA), a rare and often fatal genetic disease that causes muscle weakness and progressive loss of movement.

There are currently limited treatment options for children with SMA in the EU. Patients also receive physical aids to support muscular functions and help them and their families cope with the symptoms of the disease.

Spinal muscular atrophy is usually diagnosed in the first year of life. Most patients with severe SMA do not survive early childhood. Patients with the disease cannot produce sufficient amounts of a protein called 'survival motor neuron' (SMN), which is essential for the normal functioning and survival of motor neurons (nerves from the brain and spinal cord that control muscle movements). Without this protein, the motor neurons deteriorate and eventually die. This causes the muscles to fall into disuse, leading to muscle wasting (atrophy) and weakness.

The SMN protein is made by two genes, the SMN1 and SMN2 genes. Patients with spinal muscular atrophy lack the SMN1 gene but have the SMN2 gene, which mostly produces a 'short' SMN protein that cannot work properly on its own. A one-time intravenous administration of Zolgensma supplies a fully functioning copy of the human SMN1 gene enabling the body to produce enough SMN protein. This is expected to improve their muscle function, movement and survival of children with the disease.

Treatment with Zolgensma should only be administered once in suitable clinical centres under the supervision of a physician experienced in the management of patients with SMA.

EMA's recommendation for conditional marketing authorisation is based on the preliminary results of one completed clinical trial and three supporting studies in patients with spinal muscular atrophy with different stages of disease severity. These included genetically diagnosed and pre-symptomatic patients.

The clinical trial providing the main body of data for the assessment of Zolgensma was conducted in 22 patients who were less than six months of age at the time of the gene replacement therapy with Zolgensma. The trial assessed the percentage of patients who had improvement in their survival (i.e. without the need to be permanently on a ventilator) and motor milestones, such as head control, crawling, sitting, standing and walking (with or without assistance).

The survival of patients treated with Zolgensma exceeded what can be expected from untreated patients with severe SMA. Out of 22 patients enrolled in the trial, 20 patients (91%) were alive and did not need permanent ventilatory support at 14 months of age. The experience with this disease shows that at 14 months of age only 25% of patients are still alive. These patients also achieved motor milestones, which are usually not achieved in the natural history of the disease. 14 patients (64%) reached the milestone of independent sitting before 18 months of age. One patient (4%) reached the milestone of walking unassisted before reaching 16 months of age. Patients with less motor deterioration appeared to benefit the most from the treatment with Zolgensma.

The most common side effects found in participants in the clinical trials for Zolgensma were increases in liver enzymes (transaminases) seen in blood tests. This is an effect of the immune response to the treatment.

Because Zolgensma is an advanced-therapy medicinal product (ATMP), it was assessed by the Committee for Advanced Therapies (CAT), EMA's expert committee for cell- and gene-based medicines.

On the basis of the CAT's assessment and positive opinion, EMA's committee for human medicines (CHMP) recommended a conditional approval for this medicine. This is one of the EU's regulatory mechanisms to facilitate early access to medicines that fulfil an unmet medical need. This type of approval allows the Agency to recommend a medicine for marketing authorisation with less complete data than normally expected, in cases where the benefit of a medicine's immediate availability to patients outweighs the risk inherent in the fact that not all the data are yet available.

Additional efficacy and safety data are being collected through three ongoing studies, a long-term registry and further investigations on the product, including recommendations for future quality development. All results must be included in post-marketing safety reports, which are continuously reviewed by EMA.

Zolgensma was supported through EMA's PRIority MEdicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs. Zolgensma was granted eligibility to PRIME in January 2017 for treatment of paediatric patients diagnosed with SMA Type 1.

The opinion adopted by the CHMP is an intermediary step on Zolgensma's path to patient access. The 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. The applicant for Zolgensma is AveXis EU Limited.
2. Zolgensma is indicated for the treatment of:
   - patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or
   - patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.
3. Zolgensma was designated as an orphan medicinal product on 19 June 2015. During the development protocol assistance was received on multiple occasions to obtain guidance on the quality aspects and the clinical study programme, including the demonstration of significant benefit.

4. Following this positive CHMP opinion, the Committee for Orphan Medicinal Products (COMP) will assess whether the orphan designation should be maintained.
5. This press release was updated on 31 March 2020 to include information about EMA's PRIME scheme.
6. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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