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Questions and answers

Positive opinion on the marketing authorisation of Glybera (alipogene tiparvovec)

Opinion follows re-evaluation in a restricted group of patients

On 23 June 2011, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for Glybera for the treatment of lipoprotein lipase deficiency. The negative opinion was confirmed in October 2011, following a re-examination.

Following a request from the European Commission, the CHMP re-evaluated Glybera in a restricted group of patients with severe or multiple pancreatitis attacks. In April 2012, the CHMP maintained its previous recommendation that the medicine should not be granted a marketing authorisation. On 19 July 2012, after a second evaluation which involved the adoption of a formal opinion of the Agency's Committee for Advanced Therapies (CAT), the CHMP concluded that the medicine's benefits outweigh its risk in this patient group and recommended the granting of a marketing authorisation.

What is Glybera?

Glybera is a medicine that contains the active substance alipogene tiparvovec. It is to be available as a solution for injection.

Glybera is a type of advanced therapy medicine called a 'gene therapy product'. This is a type of medicine that works by delivering a gene into the body to correct a genetic deficiency.

What is Glybera to be used for?

Glybera is to be used to treat patients with lipoprotein lipase deficiency and who have severe or multiple pancreatitis attacks.

Lipoprotein lipase deficiency is a rare disease in which patients have a defect in the gene for lipoprotein lipase, an enzyme responsible for breaking down fats. Patients with this disease are prone to recurring attacks of pancreatitis (inflammation of the pancreas), which is a major complication.

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Glybera was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 8 March 2004 for treatment of lipoprotein lipase deficiency. More information on the orphan designation can be found here.

How is Glybera expected to work?

The active substance in Glybera, alipogene tiparvovec, is made of a virus that has been modified so it can carry a gene for lipoprotein lipase. It is to be given by injection into a muscle, where it corrects the deficiency of lipoprotein lipase by enabling cells of the muscle to produce the enzyme.

The virus used in Glybera is an 'adeno-associated viral vector' that has been modified so that it cannot make copies of itself. The virus does not cause infections in humans.

What did the company present to support its application?

The effects of Glybera were first tested in experimental models before being studied in humans. The company's clinical programme included 27 patients with lipoprotein lipase deficiency on a low-fat diet. The majority of patients who received Glybera also received immunosuppressive treatment to reduce the reaction of the body's immune system against the medicine. The main measure of effectiveness was based on a reduction in blood fat levels, with patients being followed up after the study.

What are the conclusions of the CHMP?

For the initial application, the CHMP, in consultation with the CAT, recommended in June 2011 that Glybera should not be granted authorisation, noting that there was insufficient evidence of a consistent long-lasting benefit of the medicine in the patients studied. The CHMP maintained its recommendation at the re-examination in October 2011, although at that time the CAT concluded that the concerns over the medicine's benefits could have been addressed with additional post-marketing studies.

Following the request from the European Commission, the CHMP re-evaluated Glybera in a restricted group of patients with severe or multiple pancreatitis attacks. In April 2012, the CHMP maintained its previous recommendation that the medicine should not be granted marketing authorisation[1].

The CHMP subsequently conducted a second evaluation in the restricted patient group, as it was considered that a formal CAT opinion was required. After careful consideration by both committees of all the evidence and the circumstances of the disease, including its extreme rarity, the CHMP concluded that the benefits of the medicine outweigh its risks in patients with severe or multiple pancreatitis attacks, a subgroup of severely affected patients with a high unmet medical need. The data examined indicated a reduction in the number of pancreatitis attacks which could be of benefit to these patients.

The CHMP recommended the granting of the marketing authorisation under 'exceptional circumstances'. Under the terms of the authorisation, the company will be required to provide further study data as well as data from a registry to be set up to monitor outcomes in patients treated with Glybera. There will also be in place a restricted access programme to ensure that Glybera is used appropriately.

[1] CHMP Meeting Highlights April 2012