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Questions and answers

Refusal of the marketing authorisation for Glybera

alipogene tiparvovec

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 the medicinal product Glybera, intended for use in patients with lipoprotein lipase deficiency.

The company that applied for authorisation is Amsterdam Molecular Therapeutics (AMT) B.V. It may request a re examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Glybera?

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

Glybera was developed as a type of advanced therapy medicine called a 'gene therapy product'. This is a type of medicine that works by delivering genes into the body.

What was Glybera expected to be used for?

Glybera was expected to be used in patients who lack the gene to produce lipoprotein lipase, an enzyme that is responsible for breaking down fats in lipoproteins (fat-carrying particles in the blood).

Glybera was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 8 March 2004 for treatment of lipoprotein lipase deficiency.

How is Glybera expected to work?

The active substance in Glybera, alipogene tiparvovec, is a medicinal product using a virus that has been modified so it can carry a gene for lipoprotein lipase. It was expected to be injected into the patient's muscles, where it would correct the deficiency of lipoprotein lipase by enabling the cells of the muscle to produce the enzyme.

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The virus used in Glybera is an 'adeno-associated viral vector' that has been engineered so that it cannot make copies of itself and therefore 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 presented the results of three main studies in 27 patients with lipoprotein lipase deficiency on a low-fat diet. Some patients who received Glybera also received immunosuppressive treatment to reduce the reactions of the body's immune system against medicine. The main measure of effectiveness was based on a reduction in blood fat levels, with patients being followed up for up to five years.

What were the CHMP's main concerns that led to the refusal?

Because Glybera is an advanced therapy medicine, it was assessed by the Committee for Advanced Therapies (CAT). Taking into account the assessment performed by the CAT, the CHMP concluded that the studies had not shown a consistent long-lasting benefit of Glybera. The applicant had not provided sufficient evidence of a persistence of effect in lowering blood fats in a clinically relevant manner and there were, at present, too few patients for whom sufficiently long-term data were available. There was also insufficient evidence at this stage of a reduction in the rate of pancreatitis (inflammation of the pancreas), which is a major complication of lipoprotein lipase deficiency.

In view of the uncertainty over Glybera's benefits, the CHMP was concerned about the risk associated with administration of Glybera into patients' muscles, and there were concerns about the risk associated with the use of immunosuppressive medicines during their treatment.

Whilst the CHMP considered that Glybera could be a promising treatment, the committee concluded that there was currently insufficient evidence of its benefits and safety to recommend approval at this stage. The CHMP concluded that, based on available evidence, the benefits of Glybera had not been shown to outweigh its risks and recommended that it be refused marketing authorisation.

What consequences does this refusal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that, as Glybera is administered only once, there are no consequences for people who have already received the medicine. Their doctor will continue to follow up these patients as previously agreed.

If you are in a clinical trial and need more information about your treatment, contact the doctor who has given it to you.

The summary of the opinion of the Committee for Orphan Medicinal Products for Glybera can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.