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EMA/494706/2012
Patient Health Protection

Scientific recommendation on classification of advanced therapy medicinal products

Article 17 – Regulation (EC) No 1394/2007

Disclaimer: This document is a summary for public release of a scientific recommendation on classification of advanced therapy medicinal products. The original text adopted by the Committee for Advanced Therapies (CAT) has been redacted to delete commercially confidential information.

The present scientific recommendation refers exclusively to the case as presented to the European Medicines Agency (EMA) without prejudice to future evaluations by the Agency.

This scientific recommendation is not binding and is without prejudice to any decision taken by Member State competent authorities on matters falling within their own remits.

Short descriptor (or name when available) of the proposed active substance

The active substance is a recombinant Herpes Simplex Virus type 1 (HSV-1) containing the gene encoding human granulocyte macrophage colony-stimulating factor (GM-CSF)

Brief description of the proposed finished product

The finished product is a solution for injection, intended for intralesional use, and is provided as a sterile, frozen liquid in a single-use vial.

Proposed indication

Treatment of adults with unresectable or metastatic melanoma.

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EMA/CAT comment

Consideration of Article 1(2) of Directive 2001/83/EC (definition of medicinal product – see Annex A)

- The product is presented as having properties for restoring, correcting or modifying physiological functions in human beings by exerting a pharmacological, immunological or metabolic action i.e. Treatment of adults with unresectable or metastatic melanoma;
- The active substance, in the meaning of the pharmaceutical legislation, is a recombinant Herpes Simplex Virus type 1 (HSV-1) strain containing the gene encoding human granulocyte macrophage colony-stimulating factor (hGM-CSF). GM-CSF is aimed at increasing the activity of APCs, enhancing the immune response to provide a systemic anti-tumour effect, in addition to the tumour lysis effect of the virus itself. The product is an oncolytic immunotherapy intended to be used for the treatment of adults with unresectable or metastatic melanoma. Therefore it can be considered to be a substance (as defined in Article 1(3) of Directive 2001/83/EC) with properties for treating disease in human beings.
- Based on the above considerations, it is considered that the product falls within the definition of a medicinal product (Article 1(2) of Directive 2001/83/EC).

Fulfilment of Article 2(1) of Regulation (EC) No 1394/2007 (definition of advanced therapy medicinal product – see Annex A)

- The product contains a recombinant oncolytic virus vector derived from the human wild-type HSV-1 and insertion of an expression cassette encoding the human granulocyte macrophage colony stimulating factor. This results in a recombinant virus which is non-pathogenic while providing selective replication in rapidly dividing eukaryotic cells such as tumor cells.

- The product expresses the immune stimulatory protein GM-CSF to augment the immune response against the released tumour antigens by aiding the differentiation and proliferation of dendritic cell precursors in and around the injected tumour.

- In summary the product replicates selectively in tumour cells, resulting in tumour cell lysis, and expresses GM-CSF to potentiate the immune response generated to tumour antigens released during tumour lysis.

The product consists of a recombinant virus with an exogenous human nucleic acid sequence, administered to human beings with a view to add a genetic sequence and its therapeutic effect is related directly to the product of genetic expression of this added sequence.

EMA/CAT conclusion

On the basis of the elements provided by the company and according to Article 2(1)(a) of Regulation (EC) No 1394/2007, the EMA/CAT considers that the product is an Advanced Therapy Medicinal Product (ATMP) on the basis that:

- The product is of biological origin and consists of a recombinant virus containing a recombinant nucleic acid sequence. The therapeutic effect is related directly to the product (GM-CSF) from the expression of the added sequence.
- The EMEA/CAT considers that the product falls within the definition of "Advanced Therapy Medicinal Product" as provided in Article 2(1)(a) of Regulation (EC) No 1394/2007 and more specifically falls within the classification of a Gene Therapy Medicinal Product as defined in Part IV of Annex I to Directive 2001/83/EC.