



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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

Concentrate of autologous bone marrow-derived mononuclear cells (BM-MNC).

Brief description of the proposed finished product

Suspension of concentrate of autologous bone marrow mononuclear cells (BM-MNC).

Proposed indication

Intended for improvement of heart function (LVEF) and quality of life in patients with ischaemic post acute MI and in chronic heart disease.

EMA/CAT comment

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

- The product consists of concentrate of Autologous Bone marrow-derived mononuclear cells (BM-MNC) which can be considered as a 'substance' in the meaning of the pharmaceutical legislation (in



accordance with article 1(3) of Directive 2001/83/EC), administered to humans with a view to restoring physiological function(s) by exerting a metabolic and/or a pharmacological action.

- The product is presented as having properties for treating disease and preventing further deterioration in human being.
- According to Article 1(2), the restoration, correction or modification of the physiological function is to be mediated by the substances that exert "a pharmacological, immunological or metabolic action". As the product consists of concentrate of Autologous Bone marrow-derived mononuclear cells (BM-MNC), it can be agreed that the product acts via metabolic and/or pharmacological means.

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

- The product is a preparation of concentrate of mononuclear cells (MNC) that is manufactured from Autologous Bone marrow and which is not intended to be used for the same essential function (haematological restoration). It is rather intended to be used to exert a metabolic and/or pharmacological action to prevent adverse left ventricular remodelling and further deterioration of the ischemic heart tissue, meeting the definition of "engineered" cells according to Article 2(1)(c) of Regulation (EC) No 1394/2007.
- The precise mechanisms underlying the positive outcome of these BM-MNC cells in cardiac diseases remain to be ascertained. However, regeneration through stem cell-induced angiogenesis in ischemic heart tissue by non-haematological differentiation of Bone marrow-derived mononuclear cells (BM-MNC) into vascular cells or by paracrine effects of the stem cells is the most likely mechanism. Although Bone marrow-derived mononuclear cells (BM-MNC) can locally provide a necessary microenvironment for local regeneration/cytoprotection through a metabolic actions of the cells (paracrine effects), the product can be mainly considered as a tissue engineered product as defined in Article 2(1)(b) of Regulation No 1394/2007.

Based on the above considerations, it is considered that the product falls within the definition of an advanced therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 1394/2007.

EMA/CAT conclusion

On the basis that:

- the product is a preparation of concentrate of Autologous Bone marrow-derived mononuclear cells (BM-MNC) that is not intended to be used for the same essential function (haematological restoration).
- the product is intended for regeneration through stem cell-induced angiogenesis in ischemic heart tissue by non-haematological differentiation of Bone marrow-derived mononuclear cells (BM-MNC) into vascular cells or by paracrine effects of the stem cells;

The EMEA/CAT considers that the product falls within the definition of Tissue engineered product as provided in Article 2(1) of Regulation (EC) No 1394/2007.