



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

Allogeneic bone-marrow derived osteoblastic cells.

Brief description of the proposed finished product

100,000,000 allogeneic osteoblastic cells in suspension.

Proposed indication

Treatment of non-union, delayed union or other fractures.

EMA/CAT comment

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

- The product consists of viable bone marrow–derived, *in vitro* expanded and differentiated osteoblastic cells, which can be considered a ‘substance’ in the meaning of the pharmaceutical legislation (in accordance with article 1(3) of Directive 2001/83/EC);



- The product is indicated for the treatment of non-union, delayed union or other bone fractures;
- 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 viable osteoblastic cells, it can be agreed that the product acts via metabolic means.

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

- The product is produced from viable allogeneic mesenchymal stromal cells, which are isolated from bone marrow and substantially manipulated (*in vitro* expansion and differentiation) to gain an osteoblastic cell population. Thus the active substance complies with the definition of engineered cells as described in Article 2(c) of Regulation (EC) No 1394/2007;
- The mechanism of action as claimed by the applicant, is based on the ability of the product’s cells to replace the defective or missing osteoblastic cells at their implantation site, and, via their matrix synthesis and mineralisation capacity, to regenerate and repair the defective bone tissue. Therefore, The product falls under the definition of a tissue engineered product according to Article 2(1)(b) of Regulation (EC) No 1394/2007;
- The product does not incorporate as an integral part of the product any medical devices and/or active implantable medical devices, as defined in Article 2(1)(d) of Regulation (EC) No 1394/2007.

Based on the above considerations, it is considered that the product falls within the definition of an advanced therapy medicinal product, and specifically a tissue engineered product, non-combined, as defined in Article 2(1)(a-d) of Regulation (EC) No 1394/2007.

EMA/CAT conclusion

On the basis that:

- the product is indicated for the treatment of non-union, delayed union or other bone fractures through metabolic action of the osteoblastic cells;
- the bone marrow mesenchymal stromal cells are substantially manipulated (*in vitro* expanded and differentiated) to obtain the osteoblastic cell population;
- the product is a cell suspension in pre-filled syringe and does not contain any medical devices and/or active implantable medical devices as an integral part of the product;
- the mechanism of action of the product, as claimed by the applicant, is based on the ability of the product to replace defective or missing osteoblastic and to regenerate and repair defective bone tissue,

the EMA/CAT considers that the product falls within the definition of a **tissue engineered product, non-combined**, as defined in Article 2(1)(a-d) of Regulation (EC) No 1394/2007.