



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

11 February 2013  
EMA/90882/2013  
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 isolated autologous human adipose mesenchymal stem cells, culture-expanded up to passage 4 or 5 when osteogenic differentiation and 3-dimensional structure are induced by demineralised bone matrix (DBM).

### **Brief description of the proposed finished product**

Tissue like combination of osteogenic cells and demineralised bone matrix (Three-dimensional structure of demineralised bone matrix and autologous adipose-derived and differentiated osteogenic cells).

### **Proposed indication**

The product is indicated for treatment of bone defects.



## **EMA/CAT comment**

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

- The product consists of autologous osteogenic cells and demineralised bone matrix (DBM). The product is presented as having properties for treating disease (treatment of bone defects) in human being.
- The osteogenic cells in combination with DBM can be considered 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 a physiological function (angiogenesis and osteogenesis).

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

- The product contains viable cells.
- Autologous mesenchymal stem cells derived from adipose tissue are used as one of two human-derived starting materials. The cells are subjected to various treatments, including a cell culturing step, during the manufacturing process. It can be concluded that these cells have been subject to substantial manipulation and the cells are considered to be engineered cells.
- The product is presented as having properties for bone defect treatment when used in human beings with a view to regenerating, repairing or replacing this tissue. The combination of osteogenic cells and DBM promotes angiogenesis and osteogenesis in a bone defect characterized by a lack of spontaneous bone-formation.

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

In addition, it is considered that the product does not fall within the definition of combined ATMP as provided in Article 2(1)(d) of Regulation (EC) No 1394/2007. In particular, it is noted that DBM, a human demineralised acellular collagen matrix, is primarily used as a 3-dimensional scaffold for osteogenic autologous cells. DBM is also biologically active as it potentiates the osteogenic phenotype of autologous adipose mesenchymal stem cells and induces collagen synthesis through its proteins and growth factors. DBM is an integral part of the product and, accordingly, on the basis of the information that has been made available to EMA/CAT, it cannot be considered as a medical device within the meaning of Council Directive 93/42/EEC concerning Medical Devices.

## **EMA/CAT conclusion**

On the basis that,

- the product consists of engineered cells,
- the product is presented as having properties for treating disease in human being,
- it is presented as having properties for, or is used in human beings with a view to regenerating, repairing or replacing a human tissue,

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

Additionally, the EMA/CAT considers that the product does not fall within the definition of a combined ATMP as provided in Article 2(1)(d) of Regulation (EC) No 1394/2007 as, on the basis of the information that has been made available to EMA/CAT, demineralised Bone Matrix cannot be considered a medical device within the meaning of Council Directive 93/42/EEC concerning Medical Devices.