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

Brief description of the proposed finished product

Concentrate of autologous bone marrow seeded on a matrix consisting of cross-linked bovine type-1 collagen, coated with hydroxyapatite (HA)

Proposed indication

Increase new bone formation in critical area of atrophic non-union.

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 human bone marrow cells, which can be considered a 'substance' in the meaning of the pharmaceutical legislation (in accordance with article 1(3) of Directive

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2001/83/EC) and is administered to humans with a view of restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action.

- The product is presented as having properties for treating or preventing disease in human being. CABM is to be used in Orthopaedic and traumatology to increase new bone formation in critical area of atrophic non-union.
- 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 CABM consists of viable cells seeded on a scaffold and capable of secreting therapeutic substance as well as dividing and forming new tissue, it can be agreed that the product acts via pharmacological, immunological and/or metabolic means.

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

- The product consists of viable bone marrow cells seeded on a bovine cross-linked, Type-1 collagen matrix coated with hydroxyapatite..
- The bone marrow cells aspirate containing several types of cells such as MSCs and mainly HSCs is obtained through centrifugation and followed by an incubation with a collagen matrix for a limited time prior to implantation (30 minutes). As such the cells are not considered to be substantially manipulated.
- The bovine type I collagen classified medical device in the meaning of Article 1(2)(a) of Directive 93/42/EEC, contained in the finished CABM product, temporarily replaces the anatomy of the desired bone tissue by providing a mechanically sound, 3-dimensional matrix-like template that supports cell infiltration, proliferation and, ultimately, tissue growth. As such, it is assumed that cells and the matrix form an engineered tissue-like construct where the cells are not entirely in their physiological environment.
- The product is administered to human beings with a view to increase new bone formation in the critical area of atrophic non-union. It can thus be argued that the cells or tissues is not indented to be used for the same essential functions in the recipient as in the donor.
- Hence it can be concluded that the product shall be considered 'for non-homologous use'

Based on the above considerations, it is considered that the product falls within the definition of a combined advanced therapy medicinal product.

EMA/CAT conclusion

On the basis that:

- The product consists of viable bone marrow cells seeded on the medical device (HEALOS ® biomatrix) are considered ' *for non-homologous use'* and it is *'administered to human beings with a view to regenerating, repairing or replacing a human* [bone] *tissue*'
- The EMEA/CAT considers that the product falls within the definition of a tissue engineered medicinal product as provided in Article 2(1)(b) of Regulation (EC) No 1394/2007.
- And that the type I bovine collagen, a classified medical device in the meaning of Article 1(2)(a) of Directive 93/42/EEC, contained in the finished product temporarily replaces the anatomy of the desired bone tissue by providing a mechanically sound, 3-dimensional matrix-like template that supports cell infiltration, proliferation and, ultimately, tissue growth. As the device referred to in

the application is an integral part of the product administered to patients, CABM can further be classified as a combined ATMP as defined in article 2(1)(d) of Regulation 1394/2007/EC.