25 October 2013
EMA/659840/2013
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

Human dermal fibroblasts cultured on bioresorbable polyglactin mesh

Brief description of the proposed finished product

Human dermal fibroblasts cultured on bioresorbable polyglactin mesh

Proposed indication

Treatment of wounds and ulcers

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, expanded allogeneic fibroblasts and a biodegradable PGLLA mesh, which can be considered a 'substance' in the meaning of the pharmaceutical legislation (in

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accordance with article 1(3) of Directive 2001/83/EC), administered to humans with a view to treat wounds and ulcers.

- 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 human fibroblasts, 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 expanded, viable, human fibroblasts, cultured into a biodegradable PGLLA scaffold leading to formation of a tissue equivalent with extracellular matrix (ECM). The manipulation steps are considered to alter the biological characteristics of the cells, which is required for the intended therapeutic use and thus considered substantial manipulation with regard to Annex I to Regulation (EC) No 1394/2007.

- The product is proposed for use in chronic wound indications with a view to regenerating or repairing human skin.

Based on the above considerations, it is considered that the product does fall within the definition of an advanced therapy medicinal product, and more precisely a tissue engineered product.

- The product incorporates, as an integral part, a biodegradable scaffold in accordance with Article 1(2)(a) of Directive 93/42/EEC. During the manufacturing process, the scaffold is a key component providing the correct environment for the fibroblast cells to attach, create ECM and secrete necessary growth factors and cytokines that are important for the intended therapeutic effect. The scaffold also maintains the integrity of the product to facilitate its administration in the wound bed to facilitate the mode of action for re-initiation of the healing process.

Based on the above, the product can further be classified as a Combined ATMP as defined in article 2(1)(d) of Regulation 1394/2007/EC.

EMA/CAT conclusion

On the basis that:

- The product consists of expanded, viable, human fibroblasts, cultured into a biodegradable PGLLA scaffold leading to formation of a tissue equivalent with extracellular matrix (ECM). The manipulation steps are considered to alter the biological characteristics of the cells, which is required for the intended therapeutic use and thus considered substantial manipulation with regard to Annex I to Regulation (EC) No 1394/2007
- The product is proposed for use in chronic wound indications with a view to regenerating or repairing human skin
- The product incorporates, as an integral part, a biodegradable scaffold in accordance with Article 1(2)(a) of Directive 93/42/EEC. During the manufacturing process, the scaffold is a key component providing the correct environment for the fibroblast cells to attach, create ECM and secrete necessary growth factors and cytokines that are important for the intended therapeutic effect. The scaffold also maintains the integrity of the product to facilitate its administration in the wound bed to facilitate the mode of action for re-initiation of the healing process.

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

The biodegradable scaffold is an integral part of the product and on basis of the data provided by the applicant, EMA/CAT considers that the product falls within the definition of a combined ATMP as provided in Article 2(1)(d) of Regulation (EC) No 1394/2007.