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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

Human ciliary neurotrophic factor (CNTF)

Brief description of the proposed finished product

The product is a novel, encapsulated cell-based drug delivery system which has been engineered to deliver human ciliary neurotrophic growth factor (CNTF) intraocularly after implantation via access through the sclera.

Proposed indication

The product is indicated for reducing photoreceptor loss associated with degeneration of the cells of the retina.

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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 CNTF-secreting NTC-201 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), administered to humans with a view of restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action. The product is composed of cells, which secrete a therapeutic substance to treat a disease in human beings.
- The product is presented as having properties for treating or preventing disease in human being. The product is intended for reducing photoreceptor loss associated with degeneration of the cells of the retina.
- 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 cells secreting a therapeutic substance, it can be agreed that the product acts via metabolic and pharmacological means.

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

- The product's active substance is composed of genetically engineered cells, where recombinant human CNTF- gene in the mammalian expression vector pNUT-IgSP is introduced into human retinal pigment epithelial cells through transfection. The resulting cells are further propagated through series of in vitro culture steps to yield the final drug substance. 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 cells to secrete CNTF, which in turn prevents reduction of photoreceptor loss associated with degeneration of the retina. Therefore, the product falls under the definition of a tissue engineered product according to Article 2(1)(b) of Regulation (EC) No 1394/2007. However, as the cell line has been established through transfection of a recombinant DNA containing the human CNTF gene in a mammalian expression vector, the product fulfils also the definition of a gene therapy product according to Article 2.1. of Directive (EC) No 2009/120/EC. As the product fulfils both the definitions of a tissue engineered product and a gene therapy medicinal product, the final classification should be a gene therapy medicinal product according to Article 2.5. of Regulation (EC) No 1394/2007.

- The product does incorporate as an integral part of the product two components, a semipermeable hollow fibre membrane (HFM) capsule and a scaffold of six strands of polyethylene terephthalate (PET) yarn, which fulfil the definition of a medical devices and/or active implantable medical devices, as defined in Article 2(1)(d) of Regulation (EC) No 1394/2007. Both components are required for maintenance of the cells (growth support, delivery of nutrients) and the semipermeable capsule is needed for release of the therapeutic molecule.

Based on the above considerations, it is considered that the product falls within the definition of an Advanced Therapy Medicinal Product, and specifically a gene therapy medicinal product, combined, as provided in Articles 2.1. of Directive (EC) No 2009/120/EC and Article 2.5. of Regulation (EC) No 1394/2007.

EMA/CAT conclusion

On the basis that:

- The product is indicated for reduction of photoreceptor loss associated with degeneration of the retina
- the active substance in the product is composed of genetically engineered cells, where recombinant human CNTF- gene in the mammalian expression vector pNUT-IgSP is introduced into human retinal pigment epithelial cells through transfection
- the finished product contains, as an integral part, a scaffold and a semipermeable capsule, both fulfilling the definition of a medical device and/or an active implantable medical device

the EMA/CAT considers that the product falls within the definition of a of a gene therapy medicinal product, combined, as provided in Articles 2.1. of Directive (EC) No 2009/120/EC and Article 2.5. of Regulation (EC) No 1394/2007.