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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

In vitro transcribed (IVT) ribonucleic acid (RNA)-electroporated and cultured autologous mature dendritic cells (DCs).

Brief description of the proposed finished product

Autologous dendritic cell immunotherapy consisting of autologous mature DCs co-electroporated with autologous RCC IVT RNA and synthetic CD40L IVT RNA.

* removed last paragraph in Section 'EMA/CAT comment'

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Proposed indication

Advanced renal cell carcinoma

EMA/CAT comment

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

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

- The product consists of modified autologous DC's 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 intended for the treatment of advanced renal cell carcinoma (RCC)

- 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 autologous mature DC's, it can be agreed that the product acts via pharmacological, immunological or metabolic means.

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

- The product consist of autologous cells (monocytes) which have been subjected to substantial manipulation (in vitro expansion, differentiation and RNA electroporation) to gain mature DC's that can stimulate an antigen-specific immune response. Therefore, the product fulfils the definition of advanced medicinal products as defined in Article 2(1) of regulation (EC) No 1394/ 2007.

- The product is considered not to comply with the complete requirements (part a and b) for a gene therapy medicinal product as the claim that mRNA in this case is administrated "with a view to adding a genetic sequence" is not fulfilled.

- However, it can be claimed that the product fulfils the revised definition of a somatic cell therapy medicinal product as provided in the Annex I Part IV of the Directive 2009/120/EC amending Directive 2001/83/EC as it, (a) consists of cells which has been substantially manipulated so that the biological characteristics, physiological functions or structural properties relevant for the intended clinical use of the cells have been altered and (b) is administered to human beings with a view to treating a disease through the immunological action of its cells. Therefore, the product fulfills the requirements (a) and (b) and is considered a **somatic cell therapy medicinal product.**

EMA/CAT conclusion

On the basis that,

- The product is indicated for treatment of patients with advanced renal cell carcinoma (RCC) through immunological action of the autologous mature DC's;

- The autologous mature DC's are substantially manipulated (in vitro expanded, differentiated and RNA electroporated) to elicit a specific immunostimulatory response towards the tumor in the patient.

- The mechanism of action is directly related to the expression of the mRNA encoded tumor antigens to stimulate tumor specific immune responses. The mRNA encoding CD40L is intended to modify the cells during the production process providing co-stimulatory signals. The mRNA is added ex-vivo and is not expected to be present during administration.

The EMA/CAT considers that the product falls within the definition of a **somatic cell therapy medical product** as provided in Article 2(1)(a) of Regulation (EC) No 1394/2007 and Directive 2009/120/EC Annex 1, part IV, (replacing Part IV of Annex I to Directive 2001/83/EC).