EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 September 2014
Committee for Medicinal products for Human Use (CHMP)
EMA/671958/2014

Assessment report

Procedure under Article 20 of Regulation (EC) No 726/2004

Invented name: MACI

Common name: Matrix applied characterised autologous cultured chondrocytes

Procedure number: EMEA/H/A20/1409/C/002522/0004

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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1. Background information on the procedure

On 8 September 2014, Aastrom Biosciences notified the European Medicines Agency (EMA) of the withdrawal by the Danish authorities of the manufacturing licence for the manufacturing site for the active substance, finished product and batch release of MACI (matrix-applied characterised autologous cultured chondrocytes): Genzyme Biosurgery ApS, Oliefabriksvej 45, DK - 2770 Kastrup, Denmark.

In view of the above, the European Commission initiated a procedure under Article 20 of Regulation (EC) No 726/2004 on 10 September 2014, requesting the Agency to give its opinion on whether the marketing authorisation for MACI should be suspended or revoked in accordance with Article 118 of Directive 2001/83/EC.

2. Scientific discussion

In April 2013, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP), based on a draft CHMP opinion adopted by the Committee for Advanced Therapies (CAT), recommended the authorisation of MACI (matrix applied characterised autologous cultured chondrocytes), a third generation ACI product where autologous chondrocytes are seeded onto a collagen membrane of porcine origin, which is secured into the lesion with fibrin glue. The European Commission subsequently granted Genzyme Europe B.V the marketing authorisation for MACI on 27 June 2013, for the indication of repair of symptomatic, full-thickness cartilage defects of the knee of 3-20 cm^2 in skeletally mature adult patients.

On 13 June 2014, Genzyme Europe B.V. informed the Agency of its intention to transfer the marketing authorisation to Aastrom Biosciences and to close down the only manufacturing site authorised for MACI. The Agency was also informed that following the closure of the manufacturing site, the biopsies taken from patients in the EU that have not indicated their wish not to longer receive treatment with MACI ("remaining biopsies") will be stored at the following site: 64 Sidney street, Cambridge, MA, US.

In June 2014 the CAT therefore adopted a direct healthcare professional communication (DHPC) which was subsequently endorsed by the CHMP, to inform surgeons about the planned closure of the facility and to request surgeons with biopsies stored at the manufacturing site to contact patients about their wish to finalize treatment.

On 8 August 2014, Genzyme Europe B.V. submitted an application to transfer the marketing authorisation for MACI to the Agency. Following the adoption of a CHMP opinion, the European Commission issued a decision transferring the marketing authorisation for MACI from Genzyme Europe B.V. to Aastrom Biosciences on 26 August 2014. On 5 September 2014, the Danish authorities informed Aastrom Biosciences of the withdrawal of the manufacturing licence for the manufacturing site for the active substance, finished product and batch release of MACI: Genzyme Biosurgery ApS Oliefabriksvej 45, DK - 2770 Kastrup, Denmark. At the time of the closure of the site, seven biopsies could not be processed due to outstanding feedback from patients on when and how to proceed with treatment.

In view of the above, the European Commission initiated a procedure under Article 20 of Regulation (EC) No 726/2004 on 10 September 2014, requesting the Agency to give its opinion on whether the marketing authorisation for MACI should be suspended or revoked in accordance with Article 118 of Directive 2001/83/EC.

The CHMP considered that this information did not impact the safety and efficacy profile of MACI but that in the absence of an authorised manufacturing site, the requirements laid down in Article 41 of Directive 2001/83/EC are no longer met.

3. Conclusion and grounds for the recommendation

Whereas

- The Committee considered the notification under Article 20 of Regulation (EC) No 726/2004 for MACI and the draft CHMP opinion prepared by the CAT
- The Committee concluded that in view of the absence of an authorised manufacturing site for the active substance, finished product and batch release, the requirements laid down in Article 41 of Directive 2001/83/EC are no longer met

The CHMP therefore recommends the suspension of the marketing authorisation for MACI in accordance with Article 118 of Directive 2001/83/EC.

For the suspension to be lifted, the MAH shall register a manufacturing site for the active substance, finished product and batch release (see Annex II).

In addition, the MAH should continue to ensure that all remaining biopsies are stored under appropriate conditions to allow later treatment of the relevant patients with MACI, unless the patient concerned has explicitly indicated that he/she does no longer wish treatment with MACI.

4. EPAR changes

The EPAR will be updated following the Commission Decision for this procedure under Article 20 of Regulation (EC) No 726/2004. In particular, the EPAR module 8 “steps after the authorisation” will be updated as follows:

4.1. Scope

On 8 September 2014, the MAH notified the European Medicines Agency of the withdrawal by the Danish authorities of the manufacturing licence for the manufacturing site for the active substance, finished product and batch release of MACI (matrix-applied characterised autologous cultured chondrocytes). The European Commission therefore initiated a procedure under Article 20 of Regulation (EC) No 726/2004 on 10 September 2014, requesting the Agency to give its opinion on whether the marketing authorisation for MACI should be suspended or revoked in accordance with Article 118 of Directive 2001/83/EC.

4.2. Summary

Please refer to the CHMP assessment report: MACI EMEA/H/A20/1409/C/002522/0004