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Questions and answers

Withdrawal of the marketing authorisation application for Hyalograft C autograft (characterised viable autologous chondrocytes expanded in vitro, seeded and cultured on a hyaluronan-based scaffold)

On 14 January 2013, Anika Therapeutics S.r.l. officially notified the European Medicines Agency that it wishes to withdraw its application for a marketing authorisation for Hyalograft C autograft, for repairing defects in the cartilage of the femoral condyles and trochlea (the end of the thigh bone that forms part of the knee) caused by sudden or repetitive trauma.

What is Hyalograft C autograft?

Hyalograft C autograft is an implant consisting of cartilage cells derived from the patient and planted on 2x2 cm square inserts.

Hyalograft C autograft is a type of advanced therapy product called a 'tissue engineered product'. This is a type of medicine containing cells or tissues that have been manipulated so that they can be used to repair, regenerate or replace tissue. Hyalograft C autograft is a 'combined advanced therapy product' as it incorporates a medical device (the scaffold).

What was Hyalograft C autograft being evaluated for?

Hyalograft C autograft was being evaluated for use in repairing cartilage defects at the end of the femur (the thigh bone), where the bone forms part of the knee joint. It was for use in adults experiencing symptoms caused by sudden or repetitive trauma to the cartilage.

Hyalograft C autograft has been used in the following EU countries: Austria, Bulgaria, Czech Republic, Germany, Greece, Hungary, Italy, Lithuania, Poland and Romania, before the introduction of the EU

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regulation on advanced therapies in 2009.[1] Under the regulation, advanced therapies already available in the EU are to undergo an evaluation by the EMA in order to obtain an EU wide marketing authorisation.

How does Hyalograft C autograft work?

Hyalograft C autograft is made from chondrocytes (cartilage cells) taken from the patient and grown outside the body. The cells are then planted on the square inserts, which are used by a surgeon to fill in the spaces on the bone where cartilage has been damaged.

What did the company present to support its application?

The main data submitted by the company came from two published studies involving 126 patients with femoral cartilage defects, which compared Hyalograft C autograft with a surgical technique known as microfracture repair. The main measures of effectiveness were based on the evaluation of patients' cartilage and knee function after treatment.

How far into the evaluation was the application when it was withdrawn?

The evaluation of advanced therapy products involves an assessment by the Committee for Advanced Therapies (CAT) before an opinion is adopted by the Committee for Medicinal Products for Human Use (CHMP).

This application was withdrawn after the CAT had assessed the initial documentation provided by the company and had formulated a list of questions. The company had not yet responded to the CAT's questions at the time of the withdrawal.

What was the recommendation of the CAT at that time?

At the time of the withdrawal, the CAT had not issued its final recommendation but had some concerns about the data submitted in the application. Some of the concerns were linked to the manufacturing process. There were also questions about the way the main studies were conducted, such as the failure to randomly select patients for each treatment group, which led to uncertainties about how the results should be interpreted.

Overall, the results from studies in patients did not justify the proposed use of the product and its safety could not be ascertained conclusively from the data that had so far been presented. Further data on its benefits and safety were being awaited from the company.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the company stated that the decision to withdraw the application was based on the outcome of the CAT's preliminary assessment.

The withdrawal letter is available here.

[1] Regulation (EC) No 1394/2007

What consequences does this withdrawal have for patients?

Following this withdrawal, Hyalograft C autograft will no longer be available and healthcare professionals will need to consider other treatment options for patients with femoral cartilage defects.

The company informed the EMA that there were no ongoing clinical trials or compassionate use programmes with Hyalograft C autograft at the time of the withdrawal.

Patients who have any questions should speak to their doctor.