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Questions and answers

Withdrawal of the marketing authorisation application for Imagify (perflubutane)

On 24 July 2014, Acusphere Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Imagify (perflubutane) intended to be used for diagnosing coronary heart disease.

What is Imagify?

Imagify is an imaging agent that contains the active substance perflubutane. It was to be available as a powder (lyophilisate) to be used to make a suspension for injection.

What was Imagify expected to be used for?

Imagify was expected to be used as part of a test in patients undergoing ultrasound scans of the heart (echocardiography) to find out if they have coronary heart disease, a condition in which the arteries in the heart become blocked and that can lead to a heart attack.

Imagify was to be used in patients who have stable chest pain and who are at risk of coronary heart disease. It was not intended to be used in patients who have already had a heart attack.

How is Imagify expected to work?

Imagify was to be injected into a vein before the patient undergoes echocardiography, a procedure in which sound waves are used to create images of the heart. The active substance in Imagify, which in the suspension exists as tiny bubbles of gas, reflect these sound waves, helping to form a clear image of the walls of the heart and the blood supply to the heart muscle. The images are then examined by trained personnel to determine whether or not the patient has coronary heart disease.

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What did the company present to support its application?

The company presented study data from 662 patients with chest pain who had known or suspected coronary heart disease and underwent either echocardiography using Imagify or another test known as SPECT.

Some of the patients then had a coronary angiography, which is the most accurate test available for confirming whether a patient has coronary heart disease or not but has the drawback of being an 'invasive' test, requiring the insertion of a tube (called a catheter) through a blood vessel and into the heart.

The main measure of effectiveness was how accurate the Imagify echocardiography was in detecting which patients had coronary heart disease.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the last round of questions, there were still some unresolved issues.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's response to the CHMP lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Imagify could not have been approved for use in diagnosing coronary heart disease.

The main concern of the CHMP was that the company did not provide adequate evidence that Imagify echocardiography were sufficiently sensitive or specific compared with SPECT. This means that with Imagify there could be a chance of patients with coronary heart disease being missed and patients without coronary heart disease being wrongly diagnosed as having the condition.

Therefore, the CHMP was of the opinion that the benefits of Imagify did not outweigh its risks.

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 withdrawal was based on the identification of major issues with the design of the clinical studies.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that at the time of the withdrawal there were no ongoing clinical trials or compassionate use programmes for Imagify.