European Medicines Agency

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Questions and answers on the recommendation for the refusal of the marketing authorisation for Gemesis

International Nonproprietary Name (INN): ***becaplermin***

On 23 July 2009, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Gemesis, intended for bone and periodontal (around the teeth) regeneration in adults. The company that applied for authorisation is BioMimetic Therapeutics Ltd.
The applicant requested a re-examination of the opinion. After considering the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the refusal of the marketing authorisation on 19 November 2009.

What is Gemesis?
Gemesis is a kit for implant. The kit consists of a prefilled syringe containing the active substance becaplermin and a cup containing granules of β-tricalcium phosphate to be used as a matrix.

What was Gemesis expected to be used for?
Gemesis was expected to be used to regenerate tissue in adults with defects around the teeth, including defects within the surrounding bone and receding gums.

How was Gemesis expected to work?
The active substance in Gemesis, becaplermin, is a recombinant human platelet-derived growth factor (PDGF). Growth factors are proteins that stimulate cells to multiply. Platelet-derived growth factors act on cells that are involved in wound repair. Becaplermin was expected to work in the same way as human platelet-derived growth factor, stimulating cell growth in the bone and gums around the teeth and helping tissue to heal.
Becaplermin is produced by a method known as 'recombinant DNA technology': it is made by a cell that has received a gene (DNA), which makes it able to produce human platelet-derived growth factor. Gemesis was to be prepared by mixing the solution containing becaplermin with the matrix, which was then to be placed into the defect around the teeth to promote healing.

What documentation did the company present to support its application to the CHMP?
The effects of Gemesis were first tested in experimental models before being studied in humans. In one main study involving 180 adults with advanced periodontal disease, Gemesis was compared with the matrix alone. The main measure of effectiveness was the change in 'clinical attachment level' (CAL) after 24 weeks. CAL is a measure of the loss of support to the teeth from surrounding tissue.

What were the major concerns that led the CHMP to recommend the refusal of the marketing authorisation?
The CHMP was of the opinion that the main study failed to show that Gemesis was effective in treating periodontal defects. The CHMP noted that the company did not at this time have sufficient information on how strongly becaplermin binds to PDGF receptors and did not sufficiently

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demonstrate that Gemesis used in clinical studies was comparable to the product intended to be placed on the market. The CHMP was also concerned about the level of product-related impurities present. Therefore, at that point in time, the CHMP was of the opinion that the benefits of Gemesis did not outweigh its risks. Hence, the CHMP recommended that Gemesis be refused marketing authorisation. The CHMP refusal was confirmed after re-examination.

What are the consequences of the refusal for patients in clinical trials or compassionate use programmes using Gemesis?

The company informed the CHMP that there are no patients in clinical trials or compassionate use programmes using Gemesis.