



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 February 2010
EMA/312452/2009
EMA/H/C/212/A20/33

Questions and answers on the review of Regranex (becaplermin)

Outcome of a procedure under Article 20 of Regulation (EC) No 726/2004

The European Medicines Agency has completed a review of Regranex at the request of the European Commission, following concerns about a possible risk of cancer in patients using the medicine. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of Regranex continue to outweigh its risks, but that it should not be used in patients who have cancers of any type, including skin cancer. In addition, the manufacturer has been asked to conduct more research to investigate the way the medicine is absorbed by the body and its potential risks.

What is Regranex?

Regranex is a gel that contains the active substance becaplermin. It is used together with other wound care measures to help the healing of long-term neuropathic skin ulcers (ulcers caused by a nerve problem) in people with diabetes.

The active substance in Regranex, becaplermin, is a copy of a human protein called platelet-derived growth factor-BB. Growth factors are proteins that stimulate cells to multiply. Becaplermin works in the same way as the naturally produced growth factor by stimulating cell growth and helping the growth of normal tissue for healing.

Regranex has been authorised in the European Union (EU) since 29 March 1999 and is marketed in seven Member States¹.

Why was Regranex reviewed?

In January 2009, the CHMP assessed the application for the renewal of the marketing authorisation for Regranex. The Committee concluded that, based on the available data, the benefits of Regranex continued to outweigh its risk, but that its safety should be closely monitored because of reports of cancer in a small number of patients using it. Because of this, the Committee recommended that the marketing authorisation should only be renewed for an additional five years, before being renewed again, rather than being renewed for an unlimited period.

¹ Regranex is marketed in Austria, France, Germany, Ireland, the Netherlands, Spain and the United Kingdom.



In addition, in February 2009, the company presented further results from an epidemiological study (a study of the causes and distribution of diseases in the population) that looked at the risk of cancer in patients receiving Regranex, compared with matched subjects not receiving Regranex. After reviewing these data, the CHMP was of the opinion that there was no firm evidence of a link between Regranex and cancer, but that there was also not enough evidence to rule out such a link.

Following a discussion with the European Commission on the matter, in March 2009 the Commission asked the CHMP to issue an opinion on whether the marketing authorisation for Regranex should be maintained, varied, suspended or withdrawn across the EU.

Which data has the CHMP reviewed?

The CHMP reviewed the available data on the effectiveness of Regranex, including data from the published literature. To assess its safety, the CHMP reviewed reports of side effects from studies of Regranex, as well as reports received by the company from patients, prescribers and health authorities. The CHMP also looked at the full results of the epidemiological study on the risk of cancer in patients using Regranex.

What are the conclusions of the CHMP?

The Committee noted that Regranex was modestly effective in treating neuropathic ulcers in patients with diabetes, but that its long-term effectiveness (over 20 weeks) had not been proven.

With respect to cancer, the CHMP noted that the epidemiological study suggested that the number of patients using Regranex who developed cancer was small and was not markedly different from the number of cases in patients who were not using it. The results also showed a higher number of deaths due to cancer in patients who used three or more tubes of Regranex. However, the Committee noted that, because of the way the study was designed, it was not possible to draw a firm conclusion on the risk of cancer or cancer mortality.

Based on the evaluation of currently available data and the scientific discussion within the Committee, the CHMP concluded that the benefits of Regranex continue to outweigh its risks but recommended changes to the prescribing information. The Committee recommended that Regranex must not be used by patients with any pre-existing cancer. A restriction previously applied only if the cancer was close to the area where the gel was to be applied. The full changes made to the information to doctors and patients are detailed [here](#). The Committee also asked the company to perform another epidemiological study to better evaluate the risk of cancer, as well as additional research to better characterise the extent to which the medicine is absorbed by the body.

What are the recommendations for patients?

- Patients using Regranex who have or have had cancer should speak to their doctor at a routine appointment in order to arrange alternative treatment.
- Patients should carefully follow instructions on the use of Regranex, and should raise any questions or concerns with their doctor or pharmacist.
- Prescribers should not prescribe Regranex to patients who have or have had cancer anywhere in the body.
- Prescribers should consult the latest product information before prescribing Regranex.

A European Commission decision on this opinion will be issued in due course.

The current European public assessment report for Regranex is available [here](#).