European Medicines Agency

London, 29 June 2006
Doc. Ref. EMEA/CHMP/220307/2006

QUESTIONS AND ANSWERS ON WITHDRAWAL OF MARKETING APPLICATION
for
SURFAXIN

Active substances: sinapultide, dipalmitoylphosphatidylcholine, palmitoyl-oleoyl phosphatidylglycerol and palmitic acid.

On 7 June 2006, Pharm Research Associates (UK) Limited has officially notified the Committee for Medicinal Products for Human Use (CHMP) that they wish to withdraw their marketing application for SURFAXIN, for the prevention and treatment of respiratory distress syndrome (RDS) in premature babies. SURFAXIN was designated as an 'orphan medicine' on 29 July 2004.
http://www.emea.eu.int/humandocs/PDFs/EPAR/surfaxin/21150506en.pdf

What is SURFAXIN?
SURFAXIN is a white suspension (i.e. a solution in which active substance is dissolved) to be administered into the lungs via a tube. The active substances of SURFAXIN are sinapultide, dipalmitoylphosphatidylcholine, palmitoyl-oleoyl phosphatidylglycerol and palmitic acid. It is supplied in a vial containing 8 ml of the medicinal product.

What was SURFAXIN expected to be used for?
SURFAXIN was expected to be used for the prevention of RDS in premature neonates of less than 32 weeks of gestational age (babies born 8 weeks or more too early), and, the treatment of RDS in premature neonates of less than 37 weeks of gestational age (babies born 3 weeks or more too early).
RDS is a lung disorder that causes increasing difficulty in breathing. It mainly occurs in premature babies, where the onset of difficulty in breathing is within minutes to a few hours after birth. RDS is a life-threatening disease. In infants, RDS is caused by a lack of lung surfactant; a complex of protein and fat that is normally present in lungs and helps the air sacs of the lung to inflate with air easily. The likelihood of lack of surfactant is higher in premature neonates.

How is SURFAXIN expected to work?
SURFAXIN is an artificial surfactant expected to compensate for the lack of natural surfactant in babies with RDS. It contains fat ingredients and a synthetic protein (sinapultide). The presence of synthetic ingredient prevents potential risks associated with animal-derived substance such as potential transmission of infectious agents.

What documentation was presented by the Company to support the application to the CHMP?
The effects of SURFAXIN were first tested in experimental models before being studied in humans.
The company mainly presented the results of two studies on the prevention of RDS, involving over 1,500 premature neonates in total, where SURFAXIN was compared with other surfactant agents (one which has no protein component and two others which contain animal-derived protein). Effectiveness

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 71 29
E-mail: mail@emea.eu.int http://www.emea.eu.int

was measured by looking at frequency of RDS, survival with or without related pulmonary disorder ("bronchopulmonary dysplasia"), at different points in time.

How far into the evaluation was the application when it was withdrawn?
The application was at the stage of review of answers to remaining questions, adopted at around day 180, when the Company withdrew it. After the CHMP had assessed the responses from the Company to a list of questions, there were still unresolved outstanding issues.

The CHMP normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions (at day 120), which is sent to the Company. Once the Company has supplied responses to the questions, the CHMP reviews them and may, before giving an opinion, ask any remaining question(s) (at around day 180) to the Company. Following CHMP opinion, it usually takes around 2 months for the European Commission to grant an authorisation.

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 list of questions at the time of the withdrawal, the CHMP had concerns and was of the provisional opinion that SURFAXIN could not be approved for the prevention and treatment of respiratory distress syndrome in premature babies.

What were the main concerns of the CHMP?
The main concern of the CHMP was related to the way the medicine is made, and in particular to the stability of the medicine. The CHMP was still questioning whether the design and the results of the studies were sufficient to establish that the product will be at least as effective and safe as other surfactant agents currently used to prevent RDS. Data to support the indication for the treatment of RDS were not sufficient.
Therefore, at the time of the withdrawal, the Committee's provisional view was that the benefit had not been sufficiently demonstrated and did not outweigh the identified risks.

What were the reasons given by the Company to withdraw the application?
The letter from the Company notifying the EMEA of the withdrawal of SURFAXIN is available *here*.

What are the consequences of the withdrawal for patients undergoing clinical trials / compassionate use programmes with SURFAXIN?
The company informed the EMEA that there were no ongoing clinical trials or compassionate use programmes with SURFAXIN at the time of the withdrawal.