The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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EMEA PUBLIC STATEMENT ON

INSUMAN INFUSAT 100 IU/ml solution for injection in cartridges of 3.15 ml (insulin human)

RISK OF LEAKAGE DURING USE

The European Commission granted a marketing authorisation for the European Union on 21 February 1997 for the medicinal product Insuman, which contains the active substance, recombinant human insulin. The Marketing Authorisation Holder is Hoechst Marion Roussel Deutschland GmbH, Germany, now called Aventis Pharma Deutschland GmbH. Insuman Infusat 100 IU/ml solution for injection in cartridges of 3.15 ml is marketed in Austria, France, Sweden and Finland. It is planned that Insuman Infusat is launched in the Netherlands beginning of March 2000.

Insuman is indicated for diabetes mellitus, where treatment with insulin is required. Insuman Infusat has been specially designed for use in external portable insulin pumps.

The Marketing Authorisation Holder recently informed the EMEA of 15 reports concerning leakage of cartridges used for the nationally authorised, semi-synthetic insulin for use in insulin pumps. In 12/15 cases, the cause of the leak has been identified as being a rare but apparently identical fault in the top rim of the glass cartridge. This defect has been reported with a frequency up to 1 faulty cartridge per 7,000. The same risk of leakage exists for Insuman Infusat, the recombinant insulin, because the same cartridges are used. So far, no cases of leakage have been reported with this medicinal product.
The batches of the national product affected are batches with the batch number including the letters "U" and "C" manufactured in 1998 and 1999. The batches of Insuman Infusat 100 IU/ml at risk of this defect are 40C003, 41C003, 40C004, 40C005, 40C008, 40C009, 40C010, 40C011.

In a number of the rare cases reported, it appears that insulin leaked out from the top rim of the cartridge below the metal ring and the insufficient supply of insulin led to hyperglycaemia with hospitalisation in four cases.

The risk of such a leak occurring remains very small. Patients can continue to use their present supplies provided that they pay attention to the following instructions:

- As this fault cannot be detected by a simple visual inspection on cartridges before use, patients should check, when the cartridge is in use, whether the cartridge or cartridge compartment is moist or if there is an odour of insulin. In this event the cartridge should be replaced.
- Patients should pay attention to the instructions for use of the pump.
- Patients should regularly carry out the recommended metabolism checks.

In the event of inexplicably raised blood sugar levels, the patient should check the cartridge for leaked insulin as described above. If leakage is found, the cartridge should be changed and monitoring of blood sugar levels continued. Patients will have been told under what circumstances they have to contact a doctor if they develop increased blood sugar levels. **Severe hyperglycaemia or ketoacidosis are potentially life-threatening. If the blood sugar is abnormally high patients should contact their doctor or the nearest Accident and Emergency Department immediately.**
If necessary, the physician may advise the patient to change to another insulin product.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Switchboard: (+44-20-7) 418 8400 Fax: (+44-20-7) 418 84 20
E_Mail: mail@emea.eudra.org http://www.eudra.org/emea.html

Faulty cartridges should be returned via the pharmacy or medical pump centre for further examination of the causes of the leak and to obtain a replacement.

The Marketing Authorisation Holder is currently making every effort to remedy the fault. They anticipate that they will be able to exclude this fault from their stocks and return to a normal situation by end of April 2000.

The EMEA considers it necessary to provide this new information to the public.

For further information contact:
Prof. Rolf Bass
Head of Unit of Evaluation of Medicines for Human Use
Tel: +44 207 418 8411 - Fax: +44 207 418 8420