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Questions and answers on the lack of sterility assurance with DepoCyte (cytarabine)

The European Medicines Agency has assessed the use of DepoCyte (cytarabine) following a recent inspection of the site, Pacira Pharmaceuticals Inc in San Diego, USA, where the medicine is manufactured, which highlighted deficiencies in the manufacturing process resulting in a lack of adequate sterility assurance. Although no evidence of a risk to patients has been found, the Agency's Committee for Medicinal Products for Human Use (CHMP) is recommending as a precaution that alternative treatments should be considered where available. Based on the Committee's recommendation, DepoCyte will be recalled from the market in some EU countries.

What is DepoCyte?

DepoCyte is a medicine used to treat lymphomatous meningitis, a condition in which cells from a lymphoma (a tumour in the lymphatic system) have spread to the spinal fluid and the meninges (the membranes that surround the brain and spinal cord). It is available as a sterile suspension for intrathecal injection (directly into the spinal fluid in the space that surrounds the spinal cord and the brain).

The active substance, cytarabine, is an anticancer medicine belonging to the 'anti-metabolite' group, which has been available since the 1970s. In DepoCyte, cytarabine is contained in liposomes (small fatty particles), from which the medicine is released slowly. DepoCyte treatment usually involves administration every two weeks for the first two months and then monthly as required.

DepoCyte has been authorised in the European Union since 11 July 2001 and is marketed in 18 Member States[1].

What is the problem with DepoCyte?

The Agency was informed that a recent inspection[2] of the manufacturing site, which is owned by Pacira Pharmaceuticals Inc, highlighted deficiencies in the manufacturing process of DepoCyte, relating to a lack of adequate sterility assurance. These findings pose a theoretical risk of sterility failure, even

[1] DepoCyte is currently marketed in Austria, Belgium, Bulgaria, the Czech Republic, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Poland, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom, as well as Iceland and Norway.
[2] The inspection was conducted by the UK and French medicines regulatory agencies in July 2012.

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though currently there are no data to indicate that there has been any microbial contamination of the product on the market or risk to patients.

As a result of the inspection findings, Pacira Pharmaceuticals Inc has put on hold further production and release of DepoCyte. New batches of DepoCyte will not be manufactured until issues have been resolved which will be confirmed by a re-inspection of the facilities.

What action is being taken?

Although currently there are no data indicating that the deficiencies in the manufacturing process of DepoCyte affected the sterility of the finished product on the market, the CHMP has agreed on a number of precautionary measures. The Committee recommendations take into account the availability of suitable alternative treatments.[3]

The CHMP recommends that as a precaution DepoCyte should be recalled in EU countries where suitable alternative treatments are available. However, for patients already initiated on DepoCyte and for whom alternative treatments are not appropriate, it may be possible for doctors to request a supply of DepoCyte to continue the treatment. In EU countries where no suitable alternatives exist, DepoCyte can continue to be used but with specific recommendations to monitor patients' safety.

A letter will be sent out to healthcare professionals explaining the recommendations that will apply in their country.

What are the recommendations for healthcare professionals?

- Healthcare professionals should make any treatment decision on an individual basis after discussion with the patient of potential risks associated with Depocyte if continuing treatment, or the risks with any alternative treatment and the impact of switching to an alternative, if applicable.
- In cases where DepoCyte is used, healthcare professionals should closely monitor patients who have received DepoCyte and report immediately any signs of infection, including infections of the central nervous system, which could be linked to contamination.

The current European public assessment report for DepoCyte can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.

[3] Therapeutic alternatives include medicines containing non-liposomal cytarabine, methotrexate or thiotepa. It should be noted that not all alternative products are approved for intrathecal use. For further information on indications and posology of alternative treatments, the product information should be consulted.