European Medicines Agency
Press office

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PRESS RELEASE
EMEA recommends new warnings and contraindications for ergot-derived dopamine agonists

The European Medicines Agency has recommended updating the product information for ergot-derived dopamine agonists with new warnings and contraindications in relation to the risk of fibrosis.

Ergot-derived dopamine agonists are mainly used to treat Parkinson's disease. The class comprises bromocriptine, cabergoline, dihydroergocryptine, lisuride and pergolide, all five of which are authorised at the level of the Member States.

At its June 2008 meeting, the Agency's Committee for Medicinal Products for Human Use (CHMP) finalised a review of the safety of ergot-derived dopamine agonists in relation to the risk of fibrosis (the formation of fibrous tissue in some body structures), particularly cardiac fibrosis, associated with their chronic use.

The development of the symptoms of fibrosis is a known side effect of ergot-derived dopamine agonists. However, the CHMP has reviewed new scientific data showing an increased risk of fibrosis in patients receiving ergot-derived dopamine agonists as chronic treatment, suggesting that fibrosis can start to develop far before the occurrence of symptoms.

Finalising the review of the new data the CHMP has concluded that the marketing authorisations for these medicines should be maintained, but that new warnings and contraindications should be added to their product information to reduce the risk of fibrosis.

As the risk of fibrosis is not equally established for all ergot-derived dopamine agonists, the CHMP recommended updating their prescribing information as follows:

- For cabergoline and pergolide, for which the prescribing information currently includes a contraindication for patients with evidence of valve problems and a restriction to second-line use in patients with Parkinson's disease:
  - a warning stating that patients must be monitored for signs of fibrosis with echocardiography before treatment is started and regularly during treatment;
  - a reduction of the maximum recommended dose to 3 mg per day;
  - inclusion of cardiac fibrosis as a very common side effect.

- For bromocriptine and dihydroergocryptine:
  - a contraindication for patients with pre-existing valve problems.

- For bromocriptine:
  - restriction of the maximum dose to 30 mg per day.

- For bromocriptine, dihydroergocryptine and lisuride:
  - a warning on the possible risk of fibrosis in patients taking these medicines at high doses for long periods.

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Doctors should prescribe ergot-derived dopamine agonists according to the updated prescribing information and should monitor the development of fibrosis in patients in the heart and elsewhere in the body throughout treatment. Patients should speak to their doctor or pharmacist if they have any questions.

--ENDS--

NOTES

1. More information is available in a question-and-answer document.
2. The review procedure was initiated by United Kingdom under Article 31 of Directive 2001/83/EC, as amended, following studies suggesting that the risk of cardiac fibrosis associated with the chronic use of ergot-derived dopamine agonists was greater than previously identified. An article 31 referral may be initiated in specific cases where the interest of the Community is involved. The expression 'Community interest' has a broad meaning but it refers particularly to the interests of the public health in the Community, for example following concerns related to the quality, efficacy and/or safety of a medicinal product or new pharmacovigilance information.
3. This press release, together with other information about the work of the EMEA, may be found on the EMEA web site at http://www.emea.europa.eu.

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