

30th November 2010

Osteonecrosis of the jaw in cancer patients in association with bevacizumab, Avastin[®] and concomitant or previous use of bisphosphonates

Dear Healthcare Professional

Summary

Roche Products (Ireland) Limited would like to inform you of an important update to the safety information regarding the use of AVASTIN (bevacizumab).

Cases of osteonecrosis of the jaw (ONJ) have been reported in cancer patients in association with Avastin treatment the majority of whom had received prior or concomitant treatment with i.v. bisphosphonates.

Avastin treatment may be an additional risk factor for the development of osteonecrosis of the jaw.

This potential risk should be particularly considered when Avastin and bisphosphonates are administered simultaneously or sequentially.

Dental examination and appropriate preventive dentistry should be considered prior to treatment with Avastin. In patients who have previously received or are receiving i.v. bisphosphonates invasive dental procedures should be avoided, if possible.

The communication of this information has been agreed with the European Medicines Agency (EMA) and the Irish Medicines Board (IMB).

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Further information on the safety concern

To date, it has been estimated that Avastin has been administered to more than 800,000 cancer patients.

A cumulative analysis of the company safety database, ADVENT, which includes data from clinical trials as well as spontaneous adverse drug reaction reports identified 55 cases of osteonecrosis of the jaw. Reporting rates appear to be low, less than 1 in 10,000 patients.

The majority of cases were confounded by concurrent chemotherapy and concomitant or previous bisphosphonate treatment. Many patients had also received other treatments which are known risk factors for osteonecrosis/osteonecrosis of the jaw (e.g., radiotherapy, glucocorticoids).

The occurrence of osteonecrosis of the jaw has been linked to bisphosphonate treatment. Bisphosphonates have very long half-lives and may remain active in bone tissue for many months after discontinuation of therapy.

Avastin has anti-angiogenic activity and this mechanism is currently under investigation for potential impact on the clinical course of osteonecrosis of the jaw.

The Summary of Product Characteristics for Avastin is being updated to include new safety information on osteonecrosis of the jaw (ONJ), as follows:

4.4 Special warnings and precautions for use

Cases of ONJ have been reported in cancer patients treated with Avastin, the majority of whom had received prior or concomitant treatment with i.v. bisphosphonates, for which ONJ is an identified risk. Caution should be exercised when Avastin and i.v. bisphosphonates are administered simultaneously or sequentially.

Invasive dental procedures are also an identified risk factor. A dental examination and appropriate preventive dentistry should be considered prior to starting the treatment with Avastin. In patients who have previously received or are receiving i.v. bisphosphonates invasive dental procedures should be avoided, if possible.

4.8 Undesirable Effects

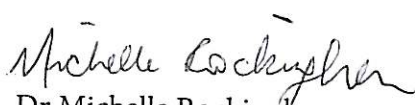
Cases of osteonecrosis of the jaw (ONJ) have been reported in patients treated with Avastin, most of which occurred in patients, who had identified risk factors for ONJ, in particular exposure to i.v. bisphosphonates and/or a history of dental disease requiring invasive dental procedures (see also section 4.4).

Call for reporting

Healthcare professionals are reminded to continue to report any serious adverse events suspected to be associated with the use of Avastin to the Drug Surveillance Centre at Roche (either by mail, telephone [01 4690700], fax [01 4690793] or e-mail [Ireland.drug_surveillance_centre@roche.com]). Alternatively, adverse events may be reported to the pharmacovigilance section of the IMB in the usual manner.

For further information or any questions on ONJ associated with the use of Avastin, please contact Medical Information at Roche (either by mail, telephone [01 4690700], fax [01 4690791] or e-mail [Ireland.druginfo@roche.com]).

Yours sincerely,


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