Roche Products (Ireland) Limited
3004 Lake Drive
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Dublin 24

Subject: **Direct Healthcare Professional Communication on Cases of Necrotising Fasciitis Reported with Avastin®**

May 15th 2013

Dear Healthcare Provider,

Roche Products (Ireland) Limited would like to inform you of the following safety information regarding the use of Avastin® (bevacizumab):

Summary

- **Necrotising fasciitis, including fatal cases, have been reported in patients receiving Avastin in both clinical trials and in the post-marketing setting.**
- **It is recommended that Avastin is discontinued and appropriate therapy initiated promptly upon diagnosis of necrotising fasciitis.**

The information in this letter has been agreed with the European Medicines Agency and the Irish Medicines Board.

Further information on the safety concern

Necrotising fasciitis is a rare but life-threatening infection of the soft tissue, characterized by rapidly spreading necrosis of superficial fascia and subcutaneous tissue. Immuno-compromised patients are at a higher risk of developing necrotising fasciitis.

The reported cases of necrotising fasciitis in Roche clinical trials and global safety database occurred in patients with several different types of cancer. Regarding associated medical conditions, the majority of the patients had gastrointestinal perforation, fistula formation or wound healing complications preceding the development of necrotising fasciitis. Some of these patients died due to complications of necrotising fasciitis.

Based on the findings, the following information will be added to section 4.4 ("Special warnings and precautions for use") of the Summary of Product Characteristics for Avastin:

"*Wound healing complications* (see section 4.8)
[...]

Necrotising fasciitis, including fatal cases, has rarely been reported in patients treated with Avastin. This condition is usually secondary to wound healing complications, gastrointestinal perforation or fistula formation. Avastin therapy should be discontinued in patients who develop necrotising fasciitis, and appropriate treatment should be promptly initiated."

This information will also be included in section 4.8 ("Undesirable effects") of the Summary of Product Characteristics for Avastin:

Table 2 Adverse reactions reported in post-marketing setting

[...]

Infections and Infestations	Necrotising fasciitis, usually secondary to wound healing complications, gastrointestinal perforation or fistula formation (rare) (see also section 4.4)

The revised Avastin product information will be made available on www.medicines.ie.

Please distribute this communication further within your team.

Call for reporting

Health care professionals should report any serious adverse events suspected to be associated with the use of Avastin to the Drug Surveillance Centre at Roche Products (Ireland) Limited (either by mail, telephone [01 4690700], fax [01 4690793] or e-mail [Ireland.drug_surveillance_centre@roche.com]). Alternatively, suspected adverse events should be reported to the Irish Medicines Board using the online form at www.imb.ie or by using the freepost yellow card system. The IMB can also be contacted on 01-6764971.

Company contact point

Should you have any questions regarding the use of Avastin, please feel free to contact Medical Information at Roche Products (Ireland) Limited (by mail, telephone [01 4690700], fax [01 4690791] or e-mail [ireland.druginfo@roche.com]).

Yours sincerely,

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