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

15th May 2013

Dear Healthcare Provider,

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

Summary

- **Necrotising fasciitis, including fatal cases, has 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 (EMA) and the Medicines Authority.

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.

Roche Products Limited	6 Falcon Way, Shire Park Welwyn Garden City	Medical Information
RXUKAVAS00169a May 2013	HERTS AL7 1TW	Tel: 0800 328 1629
	Registered in England No.100674	Email: medinfo.uk@roche.com

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 currently authorised Avastin product information is available via the Electronic Medicines Compendium at http://www.medicines.org.uk/emc

Call for reporting

Health care professionals should report any serious adverse events suspected to be associated with the use of Avastin according to national reporting requirements.

Any suspected adverse reaction should also be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Healthcare professionals should report any adverse event suspected to be associated with the use of Avastin to Roche by phone on +44 (0)1707 367554, by fax on+44 (0)1707 367582 or e-mail at welwyn.uk_dsc@roche.com.

Company contact point
Should you have any questions regarding the use of Avastin, please feel free to contact Roche Medical Information UK on 0800 328 1629 or email at medinfo.uk@roche.com

Yours sincerely,

Roche Products Ltd

Dr Julian Cole MA MRCPI Dip Pharm Med FFPM
Head of Medical Affairs (Oncology)