[redacted]
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BY EMAIL

26 September 2012

RE: Single Technology Appraisal (STA) Ranibizumab for the treatment of macular oedema caused by retinal vein occlusion (RVO) (ID328)

[redacted]

Thank you for giving us the opportunity to comments on the DSU report relating to the consideration of bevacizumab as a comparator in the appraisal of ranibizumab for the treatment of macular oedema caused by retinal vein occlusion. There is recently updated safety information from the Avastin summary of product characteristics (SPC) and package leaflet (PL) that should be considered within the DSU report to accurately depict the current data considered relevant by regulatory authorities in relation to the unlicensed use of intravitreal bevacizumab.

Avastin is not licensed, formulated or manufactured for intravitreal use, and adverse reactions have been reported from unapproved intravitreal use. Roche has no plans to seek a license for Avastin in neovascular age-related macular oedema and does not promote its use in the area.

Earlier this year the European Medicines Agency commissioned decisions to update the Avastin SPC and PL based on individual cases and clusters of serious ocular adverse events following unapproved/unlicensed intravitreal use of bevacizumab. Section 4.4 of the SPC (Special warnings and precautions for use) currently states the following:

> *"Intravitreal use*
> Avastin is not formulated for intravitreal use.
>
> *Eye disorders*
> Individual cases and clusters of serious ocular adverse events have been reported following unapproved intravitreal use of Avastin compounded from vials approved for

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intravenous administration in cancer patients. These events included infectious endophthalmitis, intraocular inflammation such as sterile endophthalmitis, uveitis and vitritis, retinal detachment, retinal pigment epithelial tear, intraocular pressure increased, intraocular haemorrhage such as vitreous haemorrhage or retinal haemorrhage and conjunctival haemorrhage. Some of these events have resulted in various degrees of visual loss, including permanent blindness.

Systemic effects following intravitreal use
A reduction of circulating VEGF concentration has been demonstrated following intravitreal anti-VEGF therapy. Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors, and there is a theoretical risk that these may relate to VEGF inhibition."

We believe this information should be communicated in the DSU report to highlight the EMA's stance in regards to intravitreal bevacizumab use.

Sincerely,

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