**Off-label intravitreal use of the medicinal product Avastin® (bevacizumab): modifications of the Summary of Product Characteristics introduced by the CHMP (Committee for Medicinal Products for Human Use) of the European Medicines Agency (EMA).**

The Italian Medicines Agency draws the attention of health professionals (physicians and pharmacists) involved in the treatment of patients with intravitreal Avastin ® (bevacizumab) on changes / additions made to section 4.4 of the Summary of Product Characteristics following by the CHMP with decision EMA/H/C/000582-II/0044 of August 30, 2012. The amendment introduced is related to reports of serious systemic adverse reactions such as non-ocular bleeding and arterial thromboembolic events following intravitreal injection of VEGF inhibitors.

In particular, section 4.4 has been updated as follows:

*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 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.

In order to ensure the safety of treated patients, AIFA recommends that physicians carefully evaluate the benefit / risk ratio for each use of the drug, informing patients about the possible risks associated with the treatment, especially for intravitreal use.

The AIFA Scientific Technical Committee (STC) in its meeting held on 26 and 27 September 2012, acquired the aforementioned updates from the CHMP (EMA), ordered:

* the removal of the indication of the use of intravitreal Avastin ® (bevacizumab) from the list referred to in Law no. 648/96 for the uses provided;
* the preparation of a specific monitoring system and collection of data on patients who will move from the use of intravitreal Avastin ® (bevacizumab) to another treatment for macular degeneration;
* the request to the Regions of data on local and systemic adverse reactions reported with the use of intravitreal Avastin ® (bevacizumab).

Therefore, the Regions will be invited to acquire the follow-up data on patients for which Avastin ® (bevacizumab) was used off-label (including use in the context of the provisions of Law 648/96) and to submit the same to AIFA by the deadline of December 31, 2012.