Dr Nicos Sarantis
Interim Medical Director

Novartis Ireland Ltd
Beech House
Beech Hill Office Campus
Clonskeagh
Dublin 4
Tel +353-1-2601255
Fax +353-1-2601263
E-Mail: nicos.sarantis
@novartis.com

NOVARTIS

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Safety Information Lucentis Meta-Analysis late-breaking news presentation at the American Academy of Ophthalmology (AAO) congress November 7, 2008 in Atlanta, USA

Novartis is writing as you are a healthcare professional involved in the management of patients with age-related macular degeneration (AMD).

With this letter we intend to share new information with you regarding the approved anti-VEGF AMD therapy, Lucentis (ranibizumab) 10 mg/ml solution for injection, which has recently been communicated to investigators participating in Lucentis clinical trials.

Novartis has informed investigators about a recent presentation at the American Academy of Ophthalmology (AAO) of a meta-analysis conducted on available 1-year and 2-year data from previous Genentech trials with Lucentis (ranibizumab) (MARINA, ANCHOR, FOCUS, PIER, SAILOR), to assess the safety of Lucentis in terms of stroke, myocardial infarction (MI) or Antiplatelet Trialists' Collaboration Arterial Thromboembolic Events (APTC ATEs[1]) overall. The main conclusions of this meta-analysis are:

- Preliminary results of the meta-analysis show a numerical difference *(not statistically significant)* towards a higher incidence rate of stroke in Lucentis 0.5mg compared with control (2 year data: 13/484 (2.7%) in patients on Lucentis vs 5/435 (1.1%) in patients on control), while no such trend was seen for MIs or APTC ATE events overall.
- The number of events was small. The 2-year incidence was lower than the 3.8% annual incidence of "any stroke" reported in the general wet-AMD population[2]. On the basis of this sole data, it is not possible to conclude (or rule out) that there is a true difference in stroke rates among the treatment groups. Further evaluations are ongoing.

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[1] APTC events include vascular deaths, nonfatal MIs, and nonfatal strokes
[2] Alexander et al, Ophthalmology, 2007, 114/12:2174-2178

- There is some suggestion that patients with risk factors for stroke (such as patients with a history of stroke) may be at increased risk of stroke when treated with Lucentis.

As Marketing Authorisation holder of Lucentis, Novartis wishes to inform you that we are currently in the process of evaluating the results presented in this meta-analysis and any other available relevant information and have informed the relevant Health Authorities.

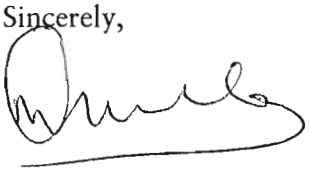
Lucentis 10 mg/ml solution for injection is approved for the treatment of wet-AMD in 75 countries. In the pivotal studies MARINA and ANCHOR, almost all Lucentis-treated patients (approximately 95%) maintained their visual acuity (defined as losing fewer than 15 letters at 12 months compared to baseline), while 34 – 40% of Lucentis-treated patients experienced a clinically significant improvement in vision (defined as gaining 15 or more letters at 12 months). These benefits were maintained over 24 months.

The recently presented meta-analysis results do not change the benefit-risk profile of Lucentis.

As patient safety is our primary concern at Novartis, we continue to closely monitor the safety profile of Lucentis and we will keep you informed. However, should you have immediate questions, please do not hesitate to contact our Medical Information officer, Agron Hasani at 01-2601255.

Call for reporting
Healthcare professionals are reminded to continue to report adverse reactions to Ann Marie Cullen at Novartis (01-2080612) or to the Pharmacovigilance Unit of the Irish Medicines Board.

Sincerely,



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