Roche

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DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

Reports of severe infectious endophthalmitis leading to blindness following the use of compounded AVASTIN® (bevacizumab) for unapproved intravitreal injection

Dear Healthcare Provider

Roche would like to inform you of important new safety information regarding unapproved intravitreal use of AVASTIN® (bevacizumab).

AVASTIN® is a recombinant humanized monoclonal antibody that is directed against the vascular endothelial growth factor (VEGF). AVASTIN® is indicated for the intravenous treatment of certain forms of cancers. However, AVASTIN® **IS NOT APPROVED FOR ANY INDICATION IN SAUDI ARABIA, INCLUDING OPHTHALMIC APPLICATIONS**.

The following important new safety information concerns the intravitreal use of AVASTIN®:

- Recently, Roche became aware of a cluster of Streptococcal endophthalmitis involving 12 patients injected within four days of each other in the area of Miami, Florida, US. The reports of infection appear to be the result of contamination following compounding AVASTIN®, although US FDA and Florida health officials continue to investigate the exact cause of the infections. Most of these patients have reported blindness or near blindness in the injected eye as a result of this infection. Additional information issued by the FDA can be found at: http://www.fda.gov/Drugs/DrugSafety/ucm270296.htm.

- Following the intravitreal use of AVASTIN®, other clusters of acute ocular inflammation and endophthalmitis have recently been reported in Los Angeles, California and Nashville, Tennessee, in the US.

- Inflammatory events, such as vitritis, uveitis, and sterile endophthalmitis, have previously been reported both as individual events and in clusters, (Following the compounding of a single vial in a large number of syringes). Some of these events have led to blindness.

- There is no indication of any change in adverse event reporting patterns from oncology patients who were treated intravenously with AVASTIN® for their cancer with manufactured lots that have been associated with these reported clusters of ocular adverse events (Lot Number 879296, 878460, 878461)

- While a causal relationship between AVASTIN® and the cluster events in Florida, Tennessee, or California has not been established, the reports are subject to ongoing analysis. Roche believes it is likely that the events of infectious endophthalmitis leading to blindness reported in Miami, Florida resulted from the repackaging of AVASTIN® without proper aseptic technique. This can compromise product sterility, potentially putting the patients at risk for microbial infections, the number of patients being affected depending on the number of syringes compounded from a single vial.

- Roche has neither studied not sought authorization for the use of AVASTIN® in ophthalmology setting.

The production methods, formulation and dosages for AVASTIN® were specifically developed for intravenous use in the oncology setting. The use of AVASTIN® in the ophthalmology setting has not been approved by any country, including Saudi Arabia. Furthermore, AVASTIN is not formulated for intravitreal use.

AVASTIN® is packaged into single-use sterile preservative free vials for intravenous use in the oncology setting; the practice of repackaging single-use AVASTIN® vials for intravitreal use into multiple aliquots may be associated with the contamination of the product.

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Call for reporting

Patient safety is a priority at Roche, and we routinely monitor the safety of our products. Healthcare professionals should report any serious adverse events suspected to be associated with the use of AVASTIN® or any of our other products at the following address through Saturday to Wednesday from 8:00 AM to 5:00 PM:

Fax: +966 2 284 7198
Phone: + 9662 2847190 Ext 131
Or by e-mail to Roche Safety mail: jeddah.drug_safety@roche.com

Alternatively, report this information to

The National Pharmacovigilance & Drug Safety Center (NPC)
Saudi Food and Drug Authority (SFDA)
Fax. +966-1-2057662
npc.drug@sfda.gov.sa

Should you have any further questions or require additional information regarding the use of AVASTIN® please feel free to contact us under the below address:

F.Hoffmann La-Roche
Najoud Centre, Gate A, 1st floor
Prince: Mohamed Bin Abdulaziz St.
Phone: +9662 2847190
Jeddah, SA

Yours sincerely,

Nasser Al-Rajhi
Scientific Office Director
17/8/2012

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