Novartis Pharma AG
Lichtstrasse 35
4056 Basel
Switzerland

Dear Healthcare Professional Communication

15 June 2021

Brolucizumab (Beovu®) - Emerging safety issue of increased incidence of Intraocular Inflammation (IOI) and related adverse events including retinal vasculitis (RV), and retinal vascular occlusion (RO) in patients with every 4 weeks dosing beyond the first three doses ("loading phase") in nAMD

Dear Healthcare Professional,

Novartis in Agreement with the Saudi Food and Drug Authority (SFDA) would like to inform you of the potential risk of increased incidence of Intraocular Inflammation (IOI) and related adverse events including retinal vasculitis (RV), and retinal vascular occlusion (RO) associated with the use of Brolucizumab (Beovu®) in patients with every 4 weeks dosing beyond the first three doses.

Summary

- **An emerging safety issue of increased incidence of Intraocular Inflammation (IOI) and related adverse events including RV, and RO in patients with every 4 weeks (q4 week) dosing beyond the first three doses in nAMD based on first interpretable results (FIR) from the CRTH258AUS04 (MERLIN) study has been observed**
- **A higher frequency of IOI including RV, and RO was noted in brolucizumab 6mg q4 week arm as compared to aflibercept 2mg q4 week**
- **You should not dose patients with Beovu 6 mg at intervals less than 8 weeks beyond the first three doses**

Background to the Urgent Safety Communication and specific details

Novartis has recently generated the FIR of the following study:

Study CRTH258AUS04 (MERLIN) is a 2-year *multicenter, randomized, double-masked Phase 3a study to assess the safety and efficacy of brolucizumab 6mg q4 week compared to aflibercept 2mg q4 week in patients with neovascular age related macular degeneration (nAMD) with persistent retinal fluid.* The study is conducted only in the US and recruited pre-treated nAMD patients with high frequency treatment need.

- The 52-week primary endpoint of non-inferiority of best corrected visual acuity (BCVA) was met for brolucizumab 6mg versus aflibercept 2 mg. The overall rate of vision loss (15 letters or more) due to any cause was 4.8% in the brolucizumab arm and 1.7% in the aflibercept arm.

- IOI including RV, and RO were reported with a higher frequency in brolucizumab 6mg q4 week arm when compared to aflibercept 2mg q4 week (9.3%vs 4.5% [RV: 0.8% vs 0.0%]; 2.0% vs 0.0%, respectively).

In the SmPC, *the recommended dose is 6 mg brolucizumab (0.05 ml solution) administered by intravitreal injection every 4 weeks (monthly) for the first 3 doses. Thereafter, the physician may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. A disease activity assessment is suggested 16 weeks (4 months) after treatment start. In patients without disease activity, treatment every 12 weeks (3 months) should be considered. In patients with disease activity, treatment every 8 weeks (2 months) should be considered. The physician may further individualise treatment intervals based on disease activity.*

In light of the emerging safety issue, **you should not dose patients with Beovu 6mg at intervals less than 8 weeks beyond the first three doses**.

Novartis is working with the health authorities to reflect the findings from the MERLIN 1-year results in revised prescribing information.

This letter has been approved by the SFDA

Call for reporting

Novartis would like to remind you to continue to report adverse reactions in accordance with the national spontaneous reporting system:

Novartis Pharma AG Patient Safety Department - Saudi Arabia -.

Toll Free Number: 8001240078
Phone: +966112658100
Fax: +966112658107
Email: adverse.events@novartis.com
Or by online: https://report.novartis.com/

Saudi Food and Drug Authority National Pharmacovigilance Center

Unified Contact Center: 19999
Fax: +966112057662
Email: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

You are also kindly requested to report the batch details for the product concerned.
Should you need any further information, please do not hesitate to contact us.

Sincerely,

Hajer Alsaleh

Country Patient Safety Manager / Novartis QPPV

Alsaleh Hager

Digitally signed by Alsaleh Hager
DN: dc=com, dc=novartis, ou=people, ou=GD, serialNumber=2495984, cn=Alsaleh Hager
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