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IMPORTANT MEDICINE SAFETY INFORMATION

17 June 2021

Dear HealthCare Professional

RE: VSIQQ® (BROLUCIZUMAB): INCREASED INCIDENCE OF INTRAOCULAR INFLAMMATION (IOI) AND RELATED ADVERSE EVENTS INCLUDING RETINAL VASCULITIS (RV), AND RETINAL VASCULAR OCCLUSION (RO) IN PATIENTS RECEIVING 4 WEEKLY DOSE AFTER THE LOADING TREATMENT

Novartis as directed by the South African Health Products Regulatory Authority (SAHPRA) would like to inform you about the increased incidence of intraocular inflammation (IOI) and related adverse events including retinal vasculitis (RV) and retinal vascular occlusion (RO) associated with Vsiqq® (brolucizumab) when administered at 4 weekly intervals beyond the first three doses.

The Professional Information (PI) of Vsiqq® will be amended to reflect the above safety information.

Summary

- A safety issue of increased incidence of IOI including RV, and RO in patients with 4 weekly dosing intervals beyond the first three doses has been observed in the MERLIN study.
- The CRTH258AUS04 (MERLIN) study is a multicenter, randomized, double-masked Phase 3a study to assess safety and efficacy of brolucizumab 6 mg q4week compared to aflibercept 2 mg q4week in patients with neovascular age-related macular degeneration (nAMD) and persistent retinal fluid (i.e., pre-treated/switch patients). A key inclusion criteria was that patients must have received at least 7 anti-VEGF intravitreal injections in the immediate 9 months prior to inclusion in the trial. This was a 104-week study with primary readout at week 52. The study was fully conducted in the United States (US). In this study a higher frequency of IOI including retinal vasculitis (RV), and retinal vascular occlusion (RO) was noted in brolucizumab 6 mg q4 week arm as compared to aflibercept 2 mg q4 week.

Background to the Urgent Safety Communication and specific details

The study was conducted only in the US and recruited pre-treated nAMD patients with high frequency treatment need. Novartis has recently generated the first interpretable results of the MERLIN study with the following assessment outcomes:

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

Advice to Healthcare Professionals

- Healthcare professionals are advised not to dose patients with Vsiqq® 6 mg at intervals less than 8 weeks beyond the first three doses**.**
- For nAMD, the recommended dose of Vsiqq® is 6 mg (0,05 ml) administered by intravitreal injection every 4 weeks (monthly) for the first three doses. Thereafter, Vsiqq® is administered every 12 weeks (3 months).
- The medical practitioner may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. The treatment interval could be as frequent as every 8 weeks (2 months).

Healthcare professionals are urged to report adverse drug reactions or product quality issues (including batch details) related to Vsiqq® to Novartis via email on patientsafety.sacg@novartis.com or website https://www.report.novartis.com. Alternatively, please complete the ADR reporting form accessible on the SAHPRA website (www.sahpra.org.za) and email it to adr@sahpra.org.za. Healthcare professionals may also use the Med Safety App [accessible from the App store (for iOS devices) and Google Play (for android devices)] or the National Department of Health Mobile Application accessible from the Essential Medicines List (EML) Clinical Guide to report ADRs or product quality issues.

For further information kindly contact Novartis as indicated below:

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Email: patientsafety.sacg@novartis.com

Sincerely,

Sequeira Dylan

Digitally signed by Sequeira Dylan
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Dylan Sequeira (RA Senior Manager)

On behalf of

Kumeshnie Padayachee

Head of Regulatory Affairs and Responsible Pharmacist