NATIONAL PBM BULLETIN

February 27, 2020

DEPARTMENT OF VETERANS AFFAIRS
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
VISN PHARMACIST EXECUTIVES (VPEs), AND THE CENTER FOR MEDICATION SAFETY (VA MedSAFE)

Alerts are based on the clinical evidence available at the time of publication. Recommendations are intended to assist practitioners in providing consistent, safe, high quality, and cost-effective drug therapy. They are not intended to interfere with clinical judgment. When using dated material, the clinician should consider new clinical information, as available and applicable.

BEOVU® (BROLUCIZUMAB-DBLL) AND RISK OF INTRAOCULAR INFLAMMATION

I. ISSUE

The American Society of Retina Specialists (ASRS) has received reports of intraocular inflammation following Beovu® (brolucizumab-dbll) administration. Cause of the inflammation is inconclusive, and the manufacturer continues to evaluate this potential risk along with further trial results.

II. BACKGROUND

Beovu® (brolucizumab-dbll) intravitreal injection is an anti-vascular endothelial growth factor (VEGF) agent indicated for the treatment of Neovascular (Wet) Age-related Macular Degeneration (AMD). Wet AMD is a chronic, degenerative ocular disorder caused by an excess of VEGF, a protein that promotes the growth of abnormal blood vessels underneath the macula. These can bleed or leak fluid, compromising retinal structure which can lead to loss of visual acuity. Per product information, administration of Beovu is contraindicated in active inflammation. Cases of intraocular inflammation submitted to ASRS occurred in patients administered a Beovu injection in the presence of residual inflammation from a previous anti-VEGF injection.

III. DISCUSSION

According to the manufacturer, approximately 46,000 injections of Beovu within the US have been administered since FDA's approval in October 2019 to date. Post-marketing reports of intraocular inflammation associated with Beovu administration have included mild-moderate cases as well as 14 cases of vasculitis, 11 of which were identified as occlusive retinal vasculitis that may threaten vision.

Phase 3 trials (HAWK/HARRIER), showed inflammation developed at a rate of 4% (32 of 730 patients) and retinal artery occlusion at a rate of ~1% (6 of 730 patients). Preliminary findings from the manufacturer's review of these study data do not suggest any predisposing factors (i.e., number of prior injections or the presence or absence of anti-Beovu neutralizing antibodies). Long-term outcomes and management strategies have not been determined.

IV. RECOMMENDATIONS

ASRS recommends that providers:

- Discuss with patients and document potential risks of intraocular inflammation associated with the use of Beovu in any informed consent.
- Inspect the eye for any intraocular inflammation immediately prior to injection of Beovu.
- Defer anti-VEGF administration when any concerning signs of inflammation are present.
- Monitor signs/symptoms of Beovu-associated inflammation with appropriate imaging due to subtle or delayed onset of occlusive vasculitis.

Providers should continue to report any adverse reactions with the use of Beovu® (brolucizumab-dbll) injection by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be

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reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800- FDA-0178, online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-_online.htm, or by mail).

V. REFERENCES

1. The American Society of Retina Specialists. Beovu Update for ASRS Members. Available at: https://www.asrs.org/clinical/clinical-updates/960/Beovu-Update-for-ASRS-Members. Accessed 02/23/20.
2. Beovu [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; October 2019.

ACTIONS

- ***Facility Director*** *(or physician designee): Forward this document to the Facility Chief of Staff (COS).*
- ***Facility COS and Chief Nurse Executives:*** *Forward this document to all appropriate providers and health care staff (e.g., **Ophthalmologists and Pharmacists, including contract providers, etc**.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*