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NIOSH Docket Office
Robert A. Taft Laboratories, MS–C34
1090 Tusculum Avenue,
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RE: (CDC-2020-0046; NIOSH-233-C) Hazardous Drugs: Draft NIOSH List of Hazardous Drugs in Healthcare Settings, 2020

Submitted via *www.regulations.gov*

The American Academy of Ophthalmology appreciates the opportunity to publicly comment on the *Hazardous Drugs: Draft NIOSH List of Hazardous Drugs in Healthcare Settings, 2020* notice and request for comment document. The Academy is concerned that NIOSH may have mistakenly listed aflibercept on the hazardous drug list. Please find our comments regarding the current use of aflibercept, dosage, occupational risk, provider burden and patient access below.

The American Academy of Ophthalmology is the largest association of eye physicians and surgeons in the United States. A nationwide community of nearly 20,000 medical doctors, we protect sight and empower lives by setting the standards for ophthalmic education and advocating for our patients and the public. We innovate to advance our profession and to ensure the delivery of the highest-quality eye care.

Current Use

Aflibercept is commonly administered in ophthalmology practices for the treatment of neovascular (wet) age related macular degeneration (wet AMD), macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), and diabetic retinopathy (DR) in patients with DME. These are serious eye conditions that cause impaired vision and blindness. Aflibercept belongs to a class of drugs called vascular endothelial growth factor (VEGF) inhibitors which are large molecule drugs. Specifically, aflibercept works by decreasing VEGF-A's activation of its native receptors, therefore reducing the subsequent growth of new blood vessels[i]. According to IRIS® Registry data, in 2019, there were nearly 4.93 million Medicare claims for intravitreal drug injections. Given the volume of claims for intravitreal injections, aflibercept is one of the most frequently used drugs to treat the indications above.

Dosage

The recommended dose for aflibercept is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months); frequency varies according to disease indication[ii].

- Wet AMD - The recommended dose for aflibercept is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months)
- RVO - The recommended dose for aflibercept is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection once every 4 weeks (monthly)
- DME and DR - The recommended dose for aflibercept is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections, followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months)

Currently, no other VEGF inhibitor used as an ocular injection is included on the hazardous drugs list, therefore we believe that aflibercept for ocular injection has mistakenly been added to the 2020 draft list.

Occupational Exposure Risk

As previously mentioned, aflibercept is a large molecule drug, one that is too large to be substantially absorbed through inhalation, ingestion, dermal or percutaneous means of exposure. Because aflibercept is supplied as one single-use, 3-mL, sterile, glass vial containing only enough drug volume to provide the 2 mg dose for the patient, the occupational exposure risk is very low. Commonly administered in ophthalmology practices across the United States, aflibercept has not resulted in accidental or occupational exposure to the knowledge of the Academy. Aflibercept has a proven safety record and ophthalmologists currently have no concern that any VEGF inhibitor used for intravitreal injection would require any additional precautions to safely handle the drug.

Increased Provider Burden Implications and Patient Access

We understand that placement on the hazardous drug list could require physicians to acquire additional personal protective equipment (PPE), which is particularly concerning given that the current COVID-19 pandemic has created barriers to procuring PPE for many medical practices. Additional PPE and handling requirements could be costly to practices and create patient access issues. When the time needed to treat a patient increases, providers are forced to reduce the number of patients that can be seen and/or increase patient wait times. We believe in the case of aflibercept that any potential increased safety measures due to placement on the hazardous drug list will not offset the provider and patient burden, causing unnecessary costs and delays in care. Due to the growing use of aflibercept and other anti-VEGF drugs, NIOSH's action has significant cost and burden implications for practices across the US.

The American Academy of Ophthalmology appreciates the opportunity to publicly comment on the *Hazardous Drugs: Draft NIOSH List of Hazardous Drugs in Healthcare Settings, 2020* notice and request for comment document. We believe aflibercept does not pose any occupational safety risks and urge NIOSH to consider the removal of aflibercept from the list of hazardous drugs. We have concerns that if aflibercept remains on the hazardous drug list patient access could be restricted and provider burden increased. We welcome a conversation with NIOSH staff on this issue. If you have additional questions, please reach out to Kayla L. Amodeo, PhD, Director of Health Policy at kamodeo@aao.org or via phone at 202-210-1797.

Sincerely,

Michael X. Repka, M.D., M.B.A.,
Medical Director, Government Affairs

[i] Papadopoulos N, Martin J, Ruan Q, et al. Binding and neutralization of vascular endothelial growth factor (VEGF) and related ligands by VEGF Trap, ranibizumab and bevacizumab. Angiogenesis. 2012;15(2):171-185. doi:10.1007/s10456-011-9249-6

[ii] https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125387lbl.pdf