October 16, 2024

Meena Seshamani, MD, PhD
Deputy Administrator and Director
Center for Medicare
Mailstop C4-26-05
7500 Security Boulevard
Baltimore, MD 21244

VIA ELECTRONIC DELIVERY

Dear Deputy Administrator Seshamani,

The American Academy of Ophthalmology (the Academy)[i] and the American Society of Retina Specialists (ASRS)[ii] are reaching out to provide notice and background around an upcoming shortage of repackaged Avastin (bevacizumab), which could challenge Medicare beneficiary access to sight-saving care. On October 11, Pine Pharmaceuticals, which as far as we know is the largest supplier of repackaged Avastin in the US, announced that they will be discontinuing production of all Avastin products (see Appendix A for the discontinuation notice).

At this time, the company has informed our organizations that they have no plans to re-enter the market and have only 2-3 weeks of supply remaining. Our organizations have significant concerns regarding patient access to repackaged Avastin and negative outcomes stemming from the abrupt discontinuation. **We ask that CMS notify all Medicare contractors, including traditional MACs and Medicare advantage plans, of this critical medication supply disruption and urge a halt to step therapy and prior authorization requirements for alternative ophthalmic anti-VEGF therapies to avoid treatment delays.**

Repackaged bevacizumab (Avastin) is the most commonly administered intravitreal drug worldwide, and therefore a disruption to its availability has a major impact on patients. This disruption is particularly concerning given the market share that Pine Pharmaceuticals has as a repackaged Avastin supplier. For ophthalmologists, particularly retina specialists, in need of repackaged Avastin for patient care, finding alternative suppliers that can provide timely access will be a significant challenge. Other U.S. Food and Drug Administration (FDA)-registered 503B outsourcing facilities, such as Leiters Health, require new customers to go through an onboarding process before new orders can be filled, which disrupts the normal flow of supply. Additionally, states such as California have few outsourcing facilities with a license allowing them to ship to their state.

Repackaged bevacizumab (Avastin) is a critically important treatment option for ophthalmology patients facing sight-threatening diseases, including age-related macular degeneration, macular edema, neovascular glaucoma and others. Avastin was first approved by the Food and Drug Administration (FDA) to treat different types of cancer. Its use in ophthalmology is considered an “off-label” use. This is the fourth major disruption to supply of repackaged Avastin in the past five years. In 2019, the efforts of

Optum (formerly Avella) to align their testing procedures with 2018 FDA final guidance, "*Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application,"* resulted in an extensive shortage. In 2021, Optum halted production of repackaged Avastin due to out-of-specification test results on select batches of the product. Last year, we experienced yet another disruption to repacked Avastin production when there was a recall at Pine Pharmaceuticals due to concerns of the FDA regarding a potential lack of sterility assurance.

Our top priority is to ensure our patients receive the highest quality care, including timely access to treatments like repackaged Avastin and any clinically appropriate alternative medications. Unexpected delays in receiving intravitreal anti-VEGF therapy has been shown to result in vision loss across multiple conditions.[iii] That is why our organizations have opposed existing step therapy policies, which interfere with the patient – physician relationship and in cases of supply instability, can create significant challenges for ophthalmology practices. Even when drug supply is stable, step therapy requirements are administratively burdensome on a physician and their staff as they help patients navigate complicated and often opaque coverage determination processes. Furthermore, payor exemption and appeals processes can be complicated and lengthy, making them onerous for strained physician practices and patients awaiting treatment.

Given the discontinuation by a major supplier and persistent access challenges in the compounded drug marketplace, it would be appropriate to halt step therapy and prior authorization requirements for repackaged Avastin alternatives. Facilitating access to alternative therapies is critical for patient care and will be a significant help to our ophthalmology practices. Additionally, if a patient must switch therapies due to the current repackaged Avastin shortage, we believe patients should be allowed to continue whichever clinically appropriate therapy they have been switched to if it is effectively treating their disease after the shortage has concluded.

We hope that CMS will take whatever steps necessary within its authority to mitigate the disruption to important sight-saving therapies. Our organizations welcome the opportunity to work with you. If you have any questions and/or to coordinate a meeting, please contact the Academy's Director of Health Policy, Brandy Keys at bkeys@aao.org or 202.587.5815, or ASRS's Vice President of Health Policy, Allison Madson at allison.madson@asrs.org or 571-213-8578.

Cc:
Cheri Rice, Deputy Director, Parts C and D, Center for Medicare

Sincerely,

Michael X. Repka, MD, MBA
Medical Director, Governmental Affairs
American Academy of Ophthalmology

Ankoor R. Shah, MD, FASRS
ASRS Practice Management
Committee Chair

[i] The American Academy of Ophthalmology is the largest association of eye physicians and surgeons in the United States. A nationwide community of over 20,000 medical doctors, we protect sight and empower lives by setting
the standards for ophthalmic education, supporting research, and advocating for our patients and the public

[ii] ASRS is the largest retina organization in the world, representing over 3,000 board certified ophthalmologists who have completed fellowship training in the medical and surgical treatment of retinal diseases. The mission of the ASRS is to provide a collegial open forum for education, to advance the understanding and treatment of vitreoretinal disease.

[iii] Song W, Singh RP, Rachitskaya AV. The Effect of Delay in Care among Patients Requiring Intravitreal Injections. Ophthalmol Retina. 2021 Oct;5(10):975-980. doi: 10.1016/j.oret.2020.12.020. Epub 2021 Jan 1. PMID: 33395587

Appendix A: Discontinuation Notice

Subject: Discontinuation of Repackaged Bevacizumab

Dear Valued Customer,

We are writing to inform you of an important change in our product offerings. Effective immediately, we are discontinuing manufacturing the below pharmaceutical products in prefilled syringes.

ITEM	DESCRIPTION
343	BEVACIZUMAB 1.25 MG/0.05 ML INJ - BD TB
963	BEVACIZUMAB 1.25MG/0.05ML INJ - SCLS MN

Prefilled syringes are designed with lubricants to ensure smooth plunger movement, which is essential for proper function. However, any visible lubricant detected during quality inspections necessitates the rejection of those units. Unfortunately, this has resulted in unsustainable batch yields, which has contributed to our decision to discontinue this product line.

We understand that the discontinuation of these syringes will cause a disruption in service, and we want to express that this decision was not made lightly. We have truly honored the opportunity to supply this drug for you and your patients over the last ten years and will continue to distribute these products while our current supplies last.

We greatly appreciate your understanding and patience during this transition. Should you have any questions or need further information, please do not hesitate to contact us at 844-218-4138 or support@pinepharmaceuticals.com.

Thank you for your understanding and continued partnership.