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February 21, 2024

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Subject: **Written Comment on LCD (L37531)- Micro-Invasive Glaucoma Surgery (MIGS)**

Dear Dr. Michael Hopkins, MD

On behalf of Allergan, an AbbVie company, the manufacturer of the XEN® Glaucoma Treatment System, we respectfully request your reconsideration on the LCD - Micro-Invasive Glaucoma Surgery (MIGS) (L37531) for a change in the LCD and one additional language change:

"This A/B MAC considers 1 XEN45 device per eye medically reasonable and necessary for the management of refractory glaucoma, defined (based upon pivotal trial criteria) as prior failure of a filtering/cilioablative procedure and/or uncontrolled intraocular pressure (IOP) (progressive damage ~~***and***~~ ***OR*** *mean diurnal medicated IOP ≥20 mmHg) on maximally tolerated medical therapy (i.e., ≥4 classes of topical IOP-lowering medications, or fewer in the case of tolerability or efficacy issues). XEN45 insertion must be performed by an ophthalmologist with experience with trabeculectomy and bleb management."* (LCD (MIGS) (L37531) effective date on 06/23/2022 page 6 of 12)

Ab Interno Gel Stent (i.e., XEN® Glaucoma Treatment System): Clinical trials evaluating the safety and effectiveness of the XEN® system with phacoemulsification are ~~***lacking***~~ ***available (Panarelli 2023; Rather 2020).*** ~~***Studies have primarily been in the form of case series with small patient populations (n=30) with short-term follow-ups (12 months) (Pérez-Torregrosa, et al., 2016).***~~(LCD (MIGS) (L37531) effective date on 06/23/2022 page 8 of 12)

Specifically, we offer information on the following for your consideration:

1. Clarification about refractory glaucoma and its implications within clinical practice
2. Summary of recent scientific data or research studies published in peer-reviewed journals or presented, including a randomized clinical trial.

Clarification refractory glaucoma and its implications within clinical practice

- According to the American Glaucoma Society (AGS) 2020 MIGS Position Paper (https://www.americanglaucomasociety.net/about/statements):
    - "Maximum tolerated medical therapy" and "refractory glaucoma" are ambiguous terms that may be confusing when integrated into clinical practice guidelines and policy statements. Differences in interpretation of these terms can also result in ambiguity in determining which patients may be eligible for different MIGS procedures. To help provide clarification, the AGS defines the terms as follows:
    - "Refractory glaucoma" is simply glaucoma that is difficult to treat and poorly controlled by current therapy, regardless of the stage of disease. Stage of disease as defined in the literature and based on the ICD-10 coding system designates the amount of damage to the visual system from glaucoma at a moment in time. All patients have a risk of progressing to worsening stages of glaucoma damage

over time if their glaucoma is not controlled. There are a variety of reasons why a particular patient's glaucoma may be difficult to treat, ranging from an inability to properly adhere to the medical management plan, inability to instill eye drops, poor responsiveness of the eye to IOP-lowering interventions, systemic side effects, or the presence of scar tissue from prior injury or surgery.

- **The XEN® 45 Gel Stent has been implanted in many patients with moderate or severe glaucoma based upon baseline IOPs < 20 mmHg,** the number of baseline IOP lowering medications <4 and from publications stating their population was moderate glaucoma patients. (Gillmann 2019; Reitsamer 2021; Ibanez-Munoz 2019; Rather 2020; Barao 2020, Panarelli 2023, Sheybani 2023)

Summary of recent scientific data or research studies published in peer-reviewed journals or presented, including a randomized clinical trial.

Robust clinical evidence has been demonstrated in over 61 clinical studies and over 4600 eyes for XEN®. The most recent publications outline below include patients that are refractory, non-refractory, and progressing. The clinical decision for further intervention was necessary to prevent detrimental long-term outcomes, namely site loss and/or blindness.

- Comparative trials evaluating clinical outcomes:
  - XEN® was compared against trabeculectomy, which is considered the gold standard for glaucoma filtering surgery. **Notable baseline patient characteristics often include IOP ≤ 20 mmHg**, ≤ 4 IOP-lowering medications and prior surgical or laser interventions. In all these trials, patients undergoing XEN® 45 Gel Stent implantation achieved similar reductions in IOP, and medication use as those receiving trabeculectomy. (Wagner 2020; Wanichwecharungruang 2021; Cappelli 2022)
- **A systematic review:**
  - A systematic review of the XEN® literature including **59 studies, with up to 36 months of follow up in more than 4,000 eyes, reported an overall range of medicated baseline IOPs of 15.3-36.1 mmHg.** (Panarelli 2023).
- A **prospective, randomized clinical trial**:
  - Effectiveness and safety of XEN® compared to trabeculectomy (mitomycin C 40mcg subconjunctival injection was used intraoperatively in both groups).
  - Patient baseline characteristics include**: IOP ranging from 15-44 mmHg,** patients receiving at least one IOP-lowering medication (mean 2.4 for XEN® and 2.1 for trabeculectomy). (Sheybani AJO 2023)

We respectfully submit for Palmetto reconsideration the request for the removal of ***~~and~~*** with replacement of ***OR*** from the statement *"…….the management of refractory glaucoma, defined as prior failure of a filtering/cilioablative procedure and/or uncontrolled intraocular pressure (IOP) defined as progressive damage* ***~~and~~*** ***OR*** *mean diurnal medicated IOP ≥20 mmHg on maximally tolerated medical therapy……"* ***and the language on the updated number of clinical trials.***

Sincerely,

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