DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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November 21, 2016

Allergan, Inc.
Ms. Barbara Niksch
Executive Director, Clinical Affairs
26970 Aliso Viejo Parkway, Suite 200
Aliso Viejo, CA 92656

Re: K161457
Trade/Device Name: Xen Glaucoma Treatment System
Regulation Number: 21 CFR 886.3920
Regulation Name: Aqueous Shunt
Regulatory Class: Class II
Product Code: KYF
Dated: October 7, 2016
Received: October 11, 2016

Dear Ms. Niksch:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kesia Alexander

for Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic and Ear,
Nose and Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161457

Device Name
Xen Glaucoma Treatment System

Indications for Use *(Describe)*
The XEN Glaucoma Treatment Systemis indicated for the management of refractory glaucomas, including cases where previous surgical treatment has failed, cases of primary open angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.

Type of Use *(Select one or both, as applicable)*

☐ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

This 510(k) summary is being submitted in accordance with the requirements of 21 CFR 807.92.

I. SUBMITTER

Allergan, Inc.
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Mail Code T2-6L
Irvine, CA 92612

Contact Person: Barbara A. Niksch
Executive Director, Clinical Affairs
Allergan, Inc.
(714) 246-6914

Date Summary Prepared: November 16, 2016

II. DEVICE

Trade Name: XEN Glaucoma Treatment System

Common Name: Glaucoma Implant

Classification Name: Aqueous shunt (21 CFR 886.3920)

Device Class: Class II (special controls)

Device Product Code: KYF ("Implant, Eye Valve")

III. PREDICATE DEVICES

- Ahmed Glaucoma Valve Implant, Model S2 (K925636)
- EX-PRESS Glaucoma Filtration Device (formerly referred to as the Ex-Press Mini Glaucoma Implant (K012852))

IV. DEVICE DESCRIPTION

The XEN Glaucoma Treatment System consists of the XEN45 Gel Stent preloaded into the XEN Injector. The XEN45 Gel Stent is composed of a gelatin derived from porcine dermis, formed into a tube, and then cross-linked with glutaraldehyde. The inside diameter of the tube is approximately 45 μm, its outside diameter is approximately 150 μm, and it has a length of approximately 6 mm. The XEN45 Gel Stent creates a permanent channel through the sclera allowing aqueous flow from the anterior chamber to the subconjunctival space.

The XEN45 Gel Stent is preloaded into an injector designed to place the XEN45 Gel Stent in the intended position. The injector with the preloaded implant is sterilized via gamma irradiation and is provided sterile. The injector is discarded after a one-time use.

V. INTENDED USE

The XEN Glaucoma Treatment System has the same intended use as the predicates and all other devices regulated within the generic type of device known as aqueous shunts in accordance with 21 CFR 886.3920. The device is a prescription (Rx) device that is intended to be permanently implanted to reduce intraocular pressure for the management of glaucoma. The XEN Glaucoma Treatment System will bear the following indications for use statement:

> *The XEN Glaucoma Treatment System is indicated for the management of refractory glaucomas, including cases where previous surgical treatment has failed, cases of primary open angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.*

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICES

The technological characteristics of the XEN Glaucoma Treatment System, the Ahmed Glaucoma Valve and the EX-PRESS Glaucoma Filtration Device are similar. Furthermore, the differences in technological characteristics that exist between the XEN Glaucoma Treatment System and both legally marketed predicate devices do not raise different questions of safety and effectiveness.

Comparison of the XEN Glaucoma Treatment System and the Predicate Devices

	XEN Glaucoma Treatment System	Ahmed Glaucoma Valve	EX-PRESS Glaucoma Filtration Device
Intended Use	To be permanently implanted to reduce intraocular pressure for the management of glaucoma	To be permanently implanted to reduce intraocular pressure for the management of glaucoma	To be permanently implanted to reduce intraocular pressure for the management of glaucoma
Indications for Use	The XEN Glaucoma Treatment System is indicated for the management of refractory glaucomas, including cases where previous surgical treatment has failed, cases of primary open angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.	The Ahmed Glaucoma Valve is indicated for the management of refractory glaucomas, where previous surgical treatment has failed, or by experience is known not to provide satisfactory results. Such refractory glaucomas can include neovascular glaucoma, primary open angle glaucoma unresponsive to medication, congenital or infantile glaucoma and refractory glaucomas resulting from aphakia or uveitis.	The EX-PRESS Glaucoma Filtration Device is intended to reduce intraocular pressure in glaucoma patients where medical and conventional surgical treatments have failed.
Rx or OTC	Rx	Rx	Rx
Permanent Implant	Yes	Yes	Yes
Mechanism of Action	Creates an outflow pathway from the anterior chamber to the subconjunctival space through which aqueous humor can flow resulting in a conjunctival bleb.	Creates a channel via a tube for aqueous flow from the anterior chamber to the subconjunctival space resulting in a bleb formed within the encapsulated polypropylene plate.	Creates an outflow pathway from the anterior chamber to the subconjunctival space through which aqueous humor can flow resulting in a conjunctival bleb.
Method of Insertion	Via a pre-loaded XEN Injector	Manual insertion with Class I surgical instruments	Via a pre-loaded EX-PRESS Delivery System (EDS)
Design	Single piece tube	Drainage tube and a valve/reservoir body	Single piece tube
Material	Porcine collagen/gelatin	Silicone drainage tube Polypropylene valve/reservoir body Silicone elastomer valve membrane	Stainless steel

	XEN Glaucoma Treatment System	Ahmed Glaucoma Valve	EX-PRESS Glaucoma Filtration Device
Size (nominal dimensions)	XEN45 Gel Stent dry dimensions: 6 mm length 45 microns inner diameter 150 microns outer diameter	Implant: 13 mm width, 16 mm length, 1.9 mm height Tube: 0.317 mm inner diameter (317 microns) and 0.635 mm outer diameter (635 microns)	Single piece tube: 2-3 mm length and 0.4 mm (400 microns) outer diameter Models R30 and R50 were originally cleared and have different flow characteristics created by different wire diameters welded into the device. The higher the number, the lower the resistance. The "30" and "50" designators refer to the size of the inner diameter in microns.
Sterile, Single-Use	Yes	Yes	Yes
Sterilization Method	Gamma	Gamma	Gamma

VII. PERFORMANCE DATA

A. Bench Testing

The nonclinical bench testing conducted on the XEN Glaucoma Treatment System included design verification and functional product testing, sterilization validation, packaging and shelf life testing, and biocompatibility testing. Results of the nonclinical testing demonstrate that the XEN Glaucoma Treatment System meets the defined specifications.

Design Verification and Functional Product Testing:

The XEN45 Gel Stent and the XEN injector were evaluated to verify that the design output met the original design input and intent. This testing was based on tests described in ANSI Z80.27, Implantable Glaucoma Devices. The results establish that the XEN Glaucoma Treatment System meets the design intent and complies with the applicable requirements.

Sterilization Validation:

The gamma irradiation sterilization method was validated using the VD_{max}^{25} method described in BS EN ISO 11137-1:2015 and BS EN ISO 11137-2:2015. Validation results demonstrate that a minimum exposure dose of 25 kGy has been substantiated for the routine sterilization of the XEN Glaucoma Treatment System to provide a 10^{-6} sterility assurance level (SAL).

Packaging and Shelf Life Testing:

The XEN Glaucoma Treatment System is labeled with an expiration date of 3 years. The shelf life study evaluated the functional performance of the XEN45 Gel Stent and the XEN injector, as well as the packaging integrity of the tray sealed with the Tyvek lid. Additional testing was completed to evaluate the impact of environmental conditioning and distribution factors. Test results confirm that the XEN45 Gel Stent and the XEN injector meet their functional requirements and the sterile barrier (package integrity) remains intact after simulated distribution and aging. This testing provides the justification for the 3-year shelf life and the maintenance of the sterile barrier.

Biocompatibility Testing

Biocompatibility of the final finished XEN Glaucoma Treatment System was demonstrated through testing in accordance with BS EN ISO 10993-1 "Biological evaluation of medical devices, Part 1: Evaluation and testing within a risk management process" (refer to the table below for a listing of all tests performed). Testing was performed for the Gel Stent material and for the injector components that have contact with the patient or the Gel Stent. All testing demonstrated that the device materials have an acceptable biocompatibility profile.

Listing of All Biocompatibility Tests Performed on All Patient Contacting Materials

Test	Results
Gel Stent Material Testing	
Cytotoxicity (MEM Elution)	Non-cytotoxic
Guinea Pig Maximization Sensitization	Non-irritant compared to negative control
Acute Systemic Toxicity (Mouse)	Non-toxic
Intraocular Irritation (Rabbit)	No evidence of irritation
Bacterial Mutagenicity – Ames Assay	Non-mutagenic
4 Week Intramuscular Implant (Rabbit)	Non-irritant compared to USP negative control
Direct Contact Cytotoxicity	Non-cytotoxic
Immunogenicity (Mouse)	Non-immunogenic
Injector Component Testing	
Cytotoxicity (MEM Elution)	Non-cytotoxic
Guinea Pig Maximization Sensitization	Non-irritant compared to negative control
Intraocular Irritation (Rabbit)	No evidence of irritation

B. Clinical Evidence Supporting Substantial Equivalence

A prospective, multi-center, single arm, open-label, clinical trial was conducted at 12 sites in the U.S. to evaluate the safety and effectiveness of the XEN45 Gel Stent in refractory glaucoma

subjects where previous filtering or cilioablative procedures failed or IOP was unresponsive to maximally tolerated medical therapy . Sixty-five subjects were implanted with the XEN45 Gel Stent and 18-month data were collected for safety.

The safety and effectiveness data from this clinical study establish, in the context of the publicly available data for the predicate devices, that there is no difference with respect to substantial equivalence in safety and effectiveness outcomes between the XEN45 Gel Stent and legally marketed predicate devices, confirming that the XEN45 Gel Stent is as safe and effective as the predicate devices.

Effectiveness

The results for the specified effectiveness outcomes (based on multiple imputations) are as follows:

- 76.3% of subjects were able to obtain a 12-month mean diurnal IOP reduction of ≥ 20% from baseline on the same or fewer IOP-lowering medications.
- The mean diurnal IOP reduction from baseline at the 12-month visit was -6.4 ± 1.1 (SE).

The results of additional analyses are as follows:

- The mean diurnal IOP at baseline for all subjects (n=65) was 25.1 (± 3.7) mmHg and the mean diurnal IOP at 12 months (using only observed data) for the 52 subjects who were seen at the 12-month visit was 15.9 (± 5.2) mmHg.
- The mean number of IOP-lowering medications at baseline was 3.5 (± 1.0) compared to 1.7 (± 1.5) medications at the 12-month visit (based on observed data)

The effectiveness data, when compared to the publicly available data for the predicate devices, demonstrate that the XEN Glaucoma Treatment System lowers IOP to similar levels as the predicate devices without raising different questions regarding effectiveness.

Safety

The most common adverse events reported prior to and including the 12-month visit were: additional glaucoma surgery with or without device explant, hypotony defined as < 6 mmHg at any time point regardless of whether there were any associated complications or sequelae related to the low pressure, IOP increase ≥ 10 mmHg from baseline, and needling procedures.

In addition to the U.S. Clinical Trial, OUS data (e.g., Grover et al, 2016 AGS abstract "Describing the Development of a Minimally Invasive Collagen Stent for Treating Glaucoma: First 975 Eyes Treated with the XEN Gel Stent," p. 86 and post-market surveillance data from the European Union and Canada) were considered for thoroughness.

When comparing the adverse event profile of the XEN45 Gel Stent to publicly available data on the legally marketed predicate devices, the XEN45 Gel Stent is as safe as the predicates and does not raise any different or unanticipated safety questions.

VIII. CONCLUSIONS

The XEN Glaucoma Treatment System has the same intended use as the legally marketed predicate devices identified in this 510(k) submission and all other aqueous shunts regulated by FDA under 21 CFR § 886.3920. The indications for use statement differs from those for the predicate devices, however, the differences do not alter the therapeutic effect of the device type and are based on clinical experience with the device. The XEN Glaucoma Treatment System's technological characteristics differ from the predicate devices, however, the differences do not raise new or different questions of safety or effectiveness. Results of the nonclinical testing demonstrate that the XEN Glaucoma Treatment System meets the defined specifications. Clinical data establish that the device effectively lowers intraocular pressure in refractory glaucoma patients demonstrating that the XEN Glaucoma Treatment System is as safe and effective as the predicate devices. In summary, the XEN Glaucoma Treatment System is substantially equivalent to the Ahmed Glaucoma Valve and the EX-PRESS Glaucoma Filtration Device when used in the management of refractory glaucoma.