NDA 21107-S30

SUPPLEMENT APPROVAL

Sebela Ireland Limited
Attention: Michael Beckelic
Associate Director,
Quality Assurance and Regulatory Compliance
645 Hembree Parkway, Suite I
Roswell, GA 30076

Dear Michael Beckelic:

Please refer to your supplemental new drug application (sNDA) dated and received June 21, 2023, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lotronex (alosetron hydrochloride) tablets.

This Prior Approval supplemental new drug application provides for proposed modifications to the approved Lotronex risk evaluation and mitigation strategy (REMS) to eliminate the elements to assure safe use. This supplement is in response to our June 8, 2023, REMS Modification Notification letter.

We have completed our review of this supplemental application, as amended. It is approved effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Lotronex (alosetron hydrochloride) was originally approved on September 2, 2010, and the most recent REMS modification was approved on January 7, 2016. The REMS consists of elements to assure safe use and a timetable for submission of assessments of the REMS.

In order to minimize burden on the healthcare delivery system of complying with the REMS, we determined that you were required to make the REMS modifications outlined in our REMS Modification Notification letter dated June 8, 2023.

Elements to Assure Safe Use: We have determined that elements to assure safe use are no longer necessary based on the following data:

- The recently reviewed REMS assessment reports have indicated acceptable knowledge and understanding among prescribers and patients related to the goal and objectives of the REMS despite an ongoing downward trend in completion of the voluntary REMS training program by prescribers.
- Adverse event reporting of ischemic colitis and serious complications of constipation has been stable, and an increase in severe outcomes has not been observed since the REMS was modified in 2016.
- An analysis of new female users of alosetron in the Sentinel Distributed Database from 2016 to 2020 found the rate of ischemic colitis for alosetron to be consistent with that listed in the Prescribing Information.
- There has been an ongoing downward trend in the utilization of all alosetron products.

Therefore, because the elements to assure safe use are no longer necessary to ensure the benefits of the drug outweigh the risks, a REMS is no longer required for Lotronex.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Jacqueline LeeHoffman, Safety Regulatory Project Manager, at (240) 402-8689.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology (DG)
Office of Immunology and Inflammation (OII)
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JOYCE A KORVICK
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