CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213801Orig1s000

PRODUCT QUALITY REVIEW(S)

FDA U.S. FOOD & DRUG ADMINISTRATION

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 213801
MYRBETRIQ GRANULES (mirabegron for extended-release oral suspension)

Assessment #1

Drug Product Name	MYRBETRIQ Granules (mirabegron for extended-release oral suspension)
Dosage Form	For extended-release oral suspension
Strength	8 mg / mL after reconstitution
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Astellas Pharma Global Development, Inc.
US agent, if applicable	Not Applicable

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original Submission (0001)	09/28/2020	All
Amendment (0004)	10/29/2020	Drug Substance, Drug Product
Amendment (0005)	10/30/2020	Biopharmaceutics
Amendment (0006)	11/06/2020	OPMA
Amendment (0007)	12/11/2020	Micro; Drug Product
Amendment (0009)	12/15/2020	Drug Product
Amendment (0014)	12/22/2020	Biopharmaceutics; Drug Product
Amendment (0021)	01/15/2021	Drug Product
Amendment (0024)	01/26/2021	OPMA; Drug Product
Amendment (0025)	02/05/2021	Drug Product
Amendment (0026)	02/09/2021	OPMA, Drug Product
Amendment (0028)	02/19/2021	OPMA; Drug Product
Amendment (0030)	03/04/2021	OPMA, Drug Product, Biopharmaceutics
Amendment (0031)	03/04/2021	Drug Product
Amendment (0032)	03/05/2021	Drug Product
Amendment (0036)	03/17/2021	Drug Product
Amendment (0037)	03/19/2021	Drug Product
Amendment (0038)	03/23/2021	Drug Product

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Sukhamaya (Sam) Bain	Donna Christner
Drug Product	Mark Seggel	Wendy Wilson-Lee
Manufacturing Process	Yong Wu	Yubing Tang
Facilities	Yong Wu	Yubing Tang
Microbiology	Jason God	Julie Nemecek
Biopharmaceutics	Assadollah Noory	Vidula Kolhatkar
Regulatory Business Process Manager	Marquita Burnett	
Application Technical Lead	Hong Cai	
Laboratory (OTR)	-	-
Environmental	Mark Seggel	Wendy Wilson-Lee
Labeling	Mark Seggel	Wendy Wilson-Lee

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

Astellas Pharmaceuticals' 505(b)(2) New Drug Application 213801, for MYRBETRIQ Granules (mirabegron for extended-release oral suspension), 8 mg/mL of mirabegron after reconstitution, is recommended for APPROVAL from the OPQ perspective.

Sufficient chemistry, manufacturing and controls information and supporting data have been provided in accordance with 21 CFR 314.50 to ensure the identity, strength, quality, purity, and bioavailability of the drug product.

The prescribing information (PI) and patient package insert (PPI) as submitted on March 23, 2021 (0038) and the labels as submitted on March 17, 2021 (0036) and March 19, 2021 (0037) are accurate, complete and comply with the requirements under 21 CFR 201.

All drug substance and product-related manufacturing, packaging and testing facilities have acceptable drug CGMP status. An overall manufacturing inspection recommendation of APPROVE was issued on March 17, 2021. The recommendation remains current as of this review.

The claimed categorical exclusion from the environmental assessment requirements under 21 CFR Part 25.31(b) is acceptable.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

The proposed drug product Myrbetriq Granules (mirabegron for extended-release oral suspension) is a new formulation of mirabegron developed for the treatment of neurogenic detrusor overactivity (NDO) for the pediatric patients aged 3 years and older. The active ingredient mirabegron is a beta-3 adrenergic agonists and approved in the US under Myrbetriq (mirabegron extended-release tablets), 25 mg and 50 mg, in June 28, 2012 (NDA 202611) for the adult patients and for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency and urinary frequency. Myrbetriq and Myrbetriq Granules are not substitutable on a milligram-per-milligram basis.

MYRBETRIQ Granules is supplied as granules in multi-dose bottles that are packaged in the aluminum pouches with desiccant. Each bottle is filled with approximately 8.3 g of yellowish white granules, which contain 830 mg of mirabegron. After reconstitution with 100 mL water, Myrbetriq Granules is pale brownish yellow to yellow oral suspension with 8 mg/mL of mirabegron. The oral suspension can facilitate the recommended

dosage which is determined based on patient weight. The liquid formulation will provide an alternative to the tablets for pediatric patients who have difficulties swallowing the tablets. (b) (4) This is considered crucial for the pediatric patients. Myrbetriq Granules has an extended-release profile. This is the result of its formulation (b) (4)

The preparation of the suspension will be performed by pharmacists at the time of dispensing to the patients. The pharmacist should also provide an appropriate oral dosing device to the patient. The instructions for reconstitution of Myrbetriq Granules by the pharmacist and the instructions for patient use are driven by the physico-chemical properties of the drug product. From the CMC perspective, the instructions for pharmacists and patients in the Prescribing Information (PI) and Patient Package Insert (PPI) are adequate to ensure the quality of the delivered doses.

The manufacturing, primary packaging and release testing of MYRBETRIQ Granules will be conducted at Astellas Pharm Tech Co., Ltd. Located at Yaizu-shi, Japan. The final packaging, labeling and release testing will be conducted at Astellas Pharma Europe B. V., Meppel, The Netherlands.

The expiration dating period is 24 months when MYRBETRIQ Granules is stored at 20ºC to 25ºC (68°F to 77°F) with excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. The maximum patient use period is 28 days after reconstitution with water when stored at 20ºC to 25ºC.

Proposed Indication(s) including Intended Patient Population	for the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older.
Duration of Treatment	As needed
Maximum Daily Dose	80 mg (10 mL)
Alternative Methods of Administration	Not Applicable

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