CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213801Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MYRBETRIQ®/MYRBETRIQ® GRANULES safely and effectively. See full prescribing information for MYRBETRIQ/MYRBETRIQ GRANULES.

MYRBETRIQ (mirabegron extended-release tablets), for oral use
MYRBETRIQ GRANULES (mirabegron for extended-release oral suspension)
Initial U.S. Approval: 2012

---------- RECENT MAJOR CHANGES ----------

Indications and Usage (1.2)	M/YYYY
Dosage and Administration (2)	M/YYYY
Warnings and Precautions, Increase in Blood Pressure (5.1)	M/YYYY

---------- INDICATIONS AND USAGE ----------

MYRBETRIQ is a beta-3 adrenergic agonist indicated for the treatment of:

- Overactive bladder (OAB) in adult patients with symptoms of urge urinary incontinence, urgency, and urinary frequency, either alone or in combination with the muscarinic antagonist solifenacin succinate. (1.1)
- Neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older and weighing 35 kg or more. (1.2)

MYRBETRIQ Granules is a beta-3 adrenergic agonist indicated for the treatment of NDO in pediatric patients aged 3 years and older. (1.2)

---------- DOSAGE AND ADMINISTRATION ----------

- MYRBETRIQ and MYRBETRIQ Granules are two different products and they are not substitutable on a milligram-per-milligram basis. Select the recommended product (MYRBETRIQ or MYRBETRIQ Granules) based on the indication and patient's weight. Do not combine MYRBETRIQ and MYRBETRIQ Granules to achieve the total dose. A recommended dosage for MYRBETRIQ Granules for adults has not been determined. (2.1)

OAB in Adults

- The recommended starting dose of MYRBETRIQ is 25 mg orally once daily, either alone or in combination with solifenacin succinate 5 mg orally once daily. (2.2)
- After 4 to 8 weeks, the MYRBETRIQ dose may be increased to 50 mg orally once daily. (2.2)

NDO in Pediatric Patients 3 Years and Older

- Pediatric Patients weighing less than 35 kg: Use MYRBETRIQ Granules: The recommended starting dose of MYRBETRIQ Granules is weight-based and administered as an extended-release oral suspension once daily. After 4 to 8 weeks, increase to the lowest effective dose without exceeding the maximum recommended dose. (2.3)
- Pediatric Patients weighing 35 kg or more: Use MYRBETRIQ or MYRBETRIQ Granules:
  - The recommended starting dosage of MYRBETRIQ is 25 mg orally once daily. After 4 to 8 weeks, the MYRBETRIQ dose may be increased to 50 mg orally once daily. (2.3)
  - The recommended starting dosage of MYRBETRIQ Granules, administered as an extended-release oral suspension, is 6 mL (48 mg) orally once daily. After 4 to 8 weeks, increase to a maximum dosage of MYRBETRIQ Granules 10 mL (80 mg) orally once daily (2.3)

Adult or Pediatric Patients with Renal or Hepatic Impairment: Refer to the full prescribing information for recommended dosage. (2.4, 2.5)
Preparation for MYRBETRIQ Granules: Refer to the full prescribing information. (2.6)

Administration

- MYRBETRIQ:
  - Adult patients: Swallow MYRBETRIQ whole with water. Do not chew, divide, or crush. Take with or without food. (2.7)
  - Pediatric patients: Swallow MYRBETRIQ whole with water. Do not chew, divide, or crush. Take with food. (2.7)
- MYRBETRIQ Granules:
  - Pediatric patients: Take MYRBETRIQ Granules prepared as an extended-release oral suspension. Take with food. (2.7)

---------- DOSAGE FORMS AND STRENGTHS ----------

- Extended-release tablets: 25 mg and 50 mg (3)
- For extended-release oral suspension: 8 mg/mL of mirabegron after reconstitution (3)

---------- CONTRAINDICATIONS ----------

Hypersensitivity to mirabegron or any inactive ingredients. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Increases in Blood Pressure: Can increase blood pressure in adult or pediatric patients. Periodically monitor blood pressure, especially in hypertensive patients. MYRBETRIQ/MYRBETRIQ Granules are not recommended in patients with severe uncontrolled hypertension. (5.1)
- Urinary Retention in Patients With Bladder Outlet Obstruction and in Patients Taking Muscarinic Antagonist Drugs for Overactive Bladder: Administer with caution in these patients because of risk of urinary retention. (5.2)
- Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with mirabegron. (5.3, 6.2)

---------- ADVERSE REACTIONS ----------

- Most commonly reported adverse reactions with MYRBETRIQ monotherapy in adult patients with OAB (> 2% and > placebo) were hypertension, nasopharyngitis, urinary tract infection, and headache. (6.1)
- Most commonly reported adverse reactions with MYRBETRIQ, in combination with solifenacin succinate in adult patients with OAB (> 2% and > placebo and > comparator), were dry mouth, urinary tract infection, constipation, and tachycardia. (6.1)
- Most commonly reported adverse reactions with MYRBETRIQ/MYRBETRIQ Granules in pediatric patients with NDO (≥ 3%) were UTI, nasopharyngitis, constipation, and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Astellas Pharma US, Inc. at 1-800-727-7003 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- Drugs Metabolized by CYP2D6: Mirabegron is a CYP2D6 inhibitor and, when used concomitantly with drugs metabolized by CYP2D6, especially narrow therapeutic index drugs, appropriate monitoring and possible dose adjustment of those drugs may be necessary. (5.4, 7.1, 12.3)
- Digoxin: When initiating a combination of mirabegron and digoxin with or without solifenacin succinate, use the lowest dose of digoxin; monitor serum digoxin concentrations to titrate digoxin dose to desired clinical effect. (7.2, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 3/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Adult Overactive Bladder (OAB)

MYRBETRIQ Monotherapy

MYRBETRIQ® is indicated for the treatment of OAB in adult patients with symptoms of urge urinary incontinence, urgency, and urinary frequency.

MYRBETRIQ Combination Therapy with Solifenacin Succinate

MYRBETRIQ, in combination with the muscarinic antagonist solifenacin succinate, is indicated for the treatment of OAB in adult patients with symptoms of urge urinary incontinence, urgency, and urinary frequency.

1.2 Pediatric Neurogenic Detrusor Overactivity (NDO)

MYRBETRIQ Granules

MYRBETRIQ® Granules is indicated for the treatment of NDO in pediatric patients aged 3 years and older.

MYRBETRIQ

MYRBETRIQ is indicated for the treatment of NDO in pediatric patients aged 3 years and older and weighing 35 kg or more.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage Information

MYRBETRIQ and MYRBETRIQ Granules are two different products and they are not substitutable on a milligram-per-milligram basis:

- Select the recommended product (MYRBETRIQ or MYRBETRIQ Granules) based on the indication and patient's weight *[see Indications and Usage (1) and Dosage and Administration (2.2, 2.3, 2.4, 2.5)]*.
- Do not combine MYRBETRIQ and MYRBETRIQ Granules to achieve the total dose.
- A recommended dosage for MYRBETRIQ Granules for adults has not been determined.

2.2 Recommended Dosage for Adult Patients with OAB

MYRBETRIQ Monotherapy

The recommended starting dosage of MYRBETRIQ is 25 mg orally once daily. If needed, increase to the maximum dosage of MYRBETRIQ 50 mg orally once daily after 4 to 8 weeks. For administration instructions, *see Dosage and Administration (2.7)*.

MYRBETRIQ Combination Therapy with Solifenacin Succinate

The recommended starting dosage for combination treatment is MYRBETRIQ 25 mg orally once daily and solifenacin succinate 5 mg orally once daily. If needed, increase to the maximum dosage of MYRBETRIQ 50 mg orally once daily after 4 to 8 weeks. Refer to the Prescribing Information for solifenacin succinate for additional information. For administration instructions, *see Dosage and Administration (2.7)*.

2.3 Recommended Dosage for Pediatric Patients Aged 3 Years and Older with NDO

For pediatric patients 3 years of age and older, select the appropriate product (MYRBETRIQ or MYRBETRIQ Granules) based on the patient's weight.

Pediatric Patients weighing less than 35 kg: Use MYRBETRIQ Granules

The recommended starting and maximum doses of MYRBETRIQ Granules, administered as extended-release oral suspension once daily *[see Dosage and Administration (2.6)]*, are shown in Table 1. The recommended dosages are determined based on patient weight. Evaluate patients periodically for potential dosage adjustment. For administration instructions, *see Dosage and Administration (2.7)*.

Table 1: MYRBETRIQ Granules Recommended Dosage for Pediatric Patients Aged 3 Years and Older Weighing Less Than 35 kg as an Extended-Release Oral Suspension (Administered Orally Once Daily)

Body Weight Range	Starting Dose	Maximum Volume
11 kg to less than 22 kg	3 mL (24 mg)	6 mL (48 mg)
22 kg to less than 35 kg	4 mL (32 mg)	8 mL (64 mg)
Greater than or equal to 35 kg	Refer to information in next section	

Pediatric Patients weighing 35 kg or more: Use MYRBETRIQ or MYRBETRIQ Granules

The recommended starting dosage of MYRBETRIQ is 25 mg orally once daily. If needed, increase to a maximum dosage of MYRBETRIQ 50 mg orally once daily after 4 to 8 weeks. For administration instructions, *see Dosage and Administration (2.7)*.

The recommended starting dosage of MYRBETRIQ Granules is 6 mL (48 mg) orally once daily. If needed, increase to a maximum dosage of MYRBETRIQ Granules 10 mL (80 mg) orally once daily after 4 to 8 weeks. For administration instructions, *see Dosage and Administration (2.7)*.

2.4 Recommended Dosage in Adult Patients with Renal or Hepatic Impairment

Dosage in Adults with Renal Impairment

The recommended dosage of MYRBETRIQ (administered orally once daily) in adult patients with renal impairment is described in Table 2 *[see Use in Specific Populations (8.6)]*. For administration instructions, *see Dosage and Administration (2.7)*.

Table 2: MYRBETRIQ Recommended Dosage in Adult Patients with Renal Impairment (Administered Orally Once Daily)

Estimated GFR[1]	Starting Dose	Maximum Dose
eGFR 30 to 89 mL/min/1.73 m^2	25 mg	50 mg
eGFR 15 to 29 mL/min/1.73 m^2	25 mg	25 mg
eGFR < 15 mL/min/1.73 m^2 or requiring dialysis	Not recommended	

1. Estimated GFR using the modification of diet in renal disease (MDRD) formula

Dosage in Adults with Hepatic Impairment

The recommended dosage of MYRBETRIQ (administered orally once daily) in adult patients with hepatic impairment is described in Table 3 *[see Use in Specific Populations (8.7)]*. For administration instructions, *see Dosage and Administration (2.7)*.

Table 3: MYRBETRIQ Recommended Dosage in Adult Patients with Hepatic Impairment (Administered Orally Once Daily)

Hepatic Impairment Classification	Starting Dose	Maximum Dose
Child-Pugh Class A (Mild hepatic impairment)	25 mg	50 mg
Child-Pugh Class B (Moderate hepatic impairment)	25 mg	25 mg
Child-Pugh Class C (Severe hepatic impairment)	Not Recommended	

2.5 Recommended Dosage in Pediatric Patients with Renal or Hepatic Impairment

For pediatric patients 3 years of age and older, select the appropriate product (MYRBETRIQ or MYRBETRIQ Granules) based on the patient's weight.

Pediatric Patients Weighing Less Than 35 kg with Renal or Hepatic Impairment: Use MYRBETRIQ Granules

Dosage in Pediatric Patients with Renal Impairment

The recommended dosage of MYRBETRIQ Granules in pediatric patients with renal impairment (administered orally once daily) is described in Table 4 *[see Use in Specific Populations (8.6)]*. For administration instructions, *see Dosage and Administration (2.7)*.

Table 4: MYRBETRIQ Granules Recommended Dosage in Pediatric Patients Aged 3 Years and Older Weighing Less Than 35 kg with Renal Impairment (Administered Orally Once Daily)

Estimated GFR[1]	Body Weight Range	Starting Dose	Maximum Dose
eGFR 30 to 89 mL/min/1.73 m^2	11 kg to less than 22 kg	3 mL (24 mg)	6 mL (48 mg)
	22 kg to less than 35 kg	4 mL (32 mg)	8 mL (64 mg)
eGFR 15 to 29 mL/min/1.73 m^2	11 kg to less than 22 kg	3 mL (24 mg)	3 mL (24 mg)
	22 kg to less than 35 kg	4 mL (32 mg)	4 mL (32 mg)
eGFR < 15 mL/min/1.73 m^2 or undergoing dialysis	Use is Not Recommended		

1. Estimate GFR using a validated eGFR estimating equation for the pediatric age range of the approved indication.

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