Safety and Tolerability Results from the PILLAR Study: A Phase IV, Double-Blind, Randomized, Placebo-Controlled Study of Mirabegron in Patients ≥65 years with Overactive Bladder-Wet

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Supplementary Table 1 – Inclusion and exclusion criteria

Inclusion criteria
Assessed at Screening: • IRB/IEC-approved written Informed Consent and privacy language as per national regulations obtained from patient/legally authorized representative prior to any study procedures • Male/female aged ≥65 years • Willing/able to complete micturition diary and questionnaires correctly • Symptoms of OAB (urinary frequency and urgency with incontinence) for ≥3 months prior to screening • Agreement not to participate in another interventional study between screening and final study visit Assessed at baseline (after run-in period): • Continued to meet above criteria • ≥1 incontinence episode and ≥3 urgency episodes (PPIUS grade 3 or 4) based on the 3-day micturition diary • ≥8 micturitions/day on average based on the 3-day micturition diary
Exclusion criteria
Assessed at Screening: • Ongoing symptoms suggestive of BOO or history of poorly controlled BOO • Post-void residual volume >150 mL • Neurogenic bladder or neurological dysfunction/injury that could affect the lower urinary tract or nerve supply • Significant stress incontinence or mixed stress/urgency incontinence with stress the predominant factor as determined by the investigator (confirmed by cough provocation test for female subjects). Patients with a history of stress incontinence under treatment could be included if cough provocation test passed • Indwelling catheter or practiced intermittent self-catheterization • Evidence of UTI. If a patient had a UTI at screening, rescreening could occur after confirmed successful treatment • Chronic inflammatory condition such as interstitial cystitis, bladder stones, previous pelvic radiation therapy, or previous/current malignant disease of the pelvic organs. • Residence in a nursing home • Likely to enter hospital or nursing home within the next 6 months due to medical instability, in the opinion of the investigator • Received intravesical injection in the past 12 months with botulinum toxin, resiniferatoxin, or capsaicin • Received electro-stimulation therapy for OAB • Began/changed a bladder training program or pelvic floor exercises <30 days prior to screening • Moderate or severe hepatic impairment (Child-Pugh Class B or C) • Severe renal impairment (estimated creatinine clearance <29 mL/min determined by eGFR; Cockcroft-Gault or MDRD formulae). Patients with ESRD or undergoing dialysis were not candidates for the study • Severe uncontrolled hypertension (sitting SBP ≥180 mmHg and/or DBP ≥110 mmHg) • Evidence of QT prolongation on ECG (QTc >450 ms for men or >470 ms for women) or a known history of QT prolongation • Clinically significant ECG abnormality, as determined by the investigator

- AST or ALT > 2x ULN or γ-GT >3x ULN and considered clinically significant by the investigator
- Hypersensitivity to any component of mirabegron, other β adrenoreceptor agonists, or any of the inactive ingredients
- Any clinically significant condition, which in the opinion of the investigator, makes the patient unsuitable for study participation
- Treated with an experimental device with 28 days or received an investigational agent within 28 days or 5 half-lives (whichever is longer) prior to screening
- Concurrent malignancy or history of any malignancy within the past 5 years, except non-metastatic basal or squamous cell carcinoma of the skin that was treated successfully
- Current history of alcohol/drug abuse
- Use of protocol-prohibited medications which could not be stopped safely within 30 days prior to screening
- Stopped, started, or changed the dose of a protocol-restricted medication within 30 days prior to screening
- An employee of Astellas, third party associated with the study, or study site team
- Previously received mirabegron

Assessed at baseline (after run-in period):

- Any exclusion criteria above (screening assessments not repeated)
- Non-compliance during placebo run-in period, defined as taking <80% or >120% of study medication

Any SBP measurement ≥180 mmHg or DBP measurement ≥110 mmHg in the 3-day diary or during the baseline visit

AST aspartate aminotransferase, *ALT* alanine aminotransferase, *BOO* bladder outlet obstruction, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *ECG* electrocardiogram, *γ-GT* gamma-glutamyl transferase, *IEC* Independent Ethics Committee, *IRB* institutional review board, *MDRD* Modification of Diet in Renal Disease, *OAB* overactive bladder syndrome, *PPIUS* Patient Perception of Intensity of Urgency Scale, *SBP* systolic blood pressure, *ULN* upper limit of normal, *UTI* urinary tract infection.