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 micturations/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.