

Mirabegron for the treatment of symptoms associated  
with overactive bladder  
ERRATUM

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Group

This document contains errata in respect of the ERG report in response to the manufacturer's factual inaccuracy check.

The table below lists the page to be replaced in the original document and the nature of the change:

<b>Page No.</b>	<b>Change</b>
10	Text amended to clarify the number of trials included in the manufacturer's mixed treatment comparison (40 in total)
146	Text amended from "The ERG notes that the impact of each sensitivity analysis on the ICERs for mirabegron 50 mg versus solifenacin 5 and 10 mg was highly variable, with ICERs ranging from £573 to the dominance of solifenacin in the comparison of mirabegron 50 mg versus solifenacin 10 mg." to "The ERG notes that the impact of each sensitivity analysis on the ICERs for mirabegron 50 mg versus solifenacin 5 and 10 mg was highly variable, with ICERs ranging from £573 to £32,572"

SCORPIO was not powered to evaluate the superiority or non-inferiority of mirabegron versus tolterodine.

The manufacturer carried out a systematic review of the literature to identify studies that could potentially inform a mixed treatment comparison (MTC). Including the three trials submitted as direct clinical evidence, the manufacturer identified publications on 40 trials in OAB evaluating interventions listed as comparators of interest in the scope and that were used to construct networks to evaluate the comparative clinical effectiveness of mirabegron. The ERG notes that the manufacturer excluded studies evaluating non-oral preparations of interventions, which the ERG considers to be a deviation from the final scope, which specified modified-release formulations of oxybutynin (available as a transdermal patch) as a comparator of interest.

## **1.2 Summary of clinical effectiveness evidence submitted by the manufacturer**

ARIES, CAPRICORN, and SCORPIO were multiple arm trials in patients with symptoms of OAB. SCORPIO and ARIES evaluated the clinical effectiveness of mirabegron at doses of 50 and 100 mg versus placebo, and CAPRICORN evaluated mirabegron at doses of 50 and 25 mg, again against placebo. The primary outcomes in the three trials were change from baseline (CFB) in frequency of micturition and in frequency of incontinence episodes. SCORPIO included an additional treatment group of an active control (tolterodine), the comparative results of which the manufacturer chose not to report as SCORPIO was not powered to evaluate the superiority or non-inferiority of mirabegron versus tolterodine. The ERG acknowledges the manufacturer's point but considers that exclusion of data from the tolterodine treatment group in SCORPIO resulted in a lack of direct evidence relevant to the decision problem.

For SCORPIO, ARIES, and CAPRICORN the manufacturer presents data on outcomes assessed based on CFB for the individual treatment groups within each trial, and the difference between mirabegron (50 mg and 25 mg) and placebo at the end point. Considering the three trials submitted as direct evidence (ARIES, CAPRICORN, and SCORPIO), mirabegron 50 mg was found to be more effective than placebo at reducing all clinical outcomes evaluated, with most differences reaching statistical significance: urinary frequency per 24 hours; frequency of incontinence per 24 hours; frequency of urgency urinary incontinence per 24 hours; level of urgency; number of urgency episodes per 24 hours; and nocturia. However, results from the tolterodine active control group from SCORPIO suggest that mirabegron 50 mg is of similar clinical effectiveness to tolterodine, with no statistically significant differences noted between the two active treatments for the outcomes reported.

The manufacturer did not perform a meta-analysis of the included trials, but presented the results of a pre-specified pooled analysis of ARIES, CAPRICORN, and SCORPIO for the comparison of

The sensitivity analyses carried out by the ERG indicated that the manufacturer's primary base case cost-effectiveness result was generally robust with respect to the areas of uncertainty identified in the ERG's critique (Table 77). However, as a result of a paucity of data, the ERG were unable to assess the impact of using AE-specific (rather than other cause) immediate discontinuation rates. Although, the primary cost-effectiveness result has been demonstrated to be robust to alternative estimates of discontinuation (see Section 5.2.10).

Following individual and cumulative application of the ERG's sensitivity analyses, the ICERs estimated by the manufacturer for the individual comparisons considered in the secondary base case remained relatively consistent; with the exception of comparisons between mirabegron 50 mg and solifenacin 5 and 10 mg (Table 78). The ERG notes that the impact of each sensitivity analysis on the ICERs for mirabegron 50 mg versus solifenacin 5 and 10 mg was highly variable, with ICERs ranging from £573 to £32,572. Similarly, ICERs ranged from £11,778 to £32,572 upon application of the ERG's sensitivity analyses to the comparison of mirabegron 50 mg versus solifenacin 5 mg. Moreover, the cumulative impact of the ERG's sensitivity analyses on the comparison of mirabegron 50 mg with solifenacin 5 and 10 mg, resulted in ICER increases of £20,218 (from £12,493 to £32,711.50) and £1,573 (from £340 to £1,913), respectively.

Regarding the impact of the ERG's sensitivity analyses on the manufacturer's incremental secondary base case cost-effectiveness results; the ERG notes that, following simultaneous application of the ERG's sensitivity analyses, tolterodine ER 4 mg and solifenacin 10 mg move from being extendedly dominated by mirabegron 50 mg to being strictly dominated by solifenacin 5 mg (Table 79). Moreover, the ICER of mirabegron 50 mg versus solifenacin 5 mg increases from £12,493 to £32,712. Furthermore, the ERG notes that the ERG's revised ICER of mirabegron 50 mg versus solifenacin 5 mg (£32,712) is based on clinical effectiveness estimates from the manufacturer's MTC. As discussed in Section 4.4.2, as a result of ERG concern regarding the level of heterogeneity present in the manufacturer's MTC, the ERG carried out a revised MTC using a more homogeneous data set. However, the manufacturer's model structure did not facilitate implementation of data obtained from the ERG's MTC (i.e. the manufacturer's model used calibrated beta coefficients rather than relative estimates such as hazard ratios or odds ratios); therefore, the ERG were unable to quantify the impact of incorporating clinical effectiveness estimates from the ERG's MTC into the economic model. However, the ERG notes that estimates obtained from the ERG's MTC indicate that solifenacin 5 mg is statistically significantly more effective at reducing incontinence episodes than mirabegron 50 mg (mean difference [95% CrI]: -0.386[-0.717 to -0.055]). By contrast, estimates obtained from the manufacturer's MTC detected no statistically significant difference between solifenacin 5 mg and mirabegron 50 mg in reducing the number of incontinence episodes experienced per 24 hours (mean difference [95% CrI]: -0.237 [-0.482 to 0.007]). Based on this, the ERG considers that the ERG's revised ICER for the comparison of mirabegron 50 mg with solifenacin 5 mg is likely to be conservative; i.e. an ICER estimated using ERG MTC data is likely to be higher than £32,712.