Comment on: update on the management of overactive bladder

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Dear Editor,

Fontaine *et al.*[1] recently provided an update on the management of overactive bladder (OAB). However, the most recently approved OAB drug, vibegron, and the most recently published data supporting that approval were not addressed. I would like to take this opportunity to provide an accurate representation of vibegron and its place in the OAB treatment paradigm.

In their overview of pharmacotherapy, vibegron is mis-named as virabegron; while this may be a case of a minor typo, this may cause readers to conflate vibegron and mirabegron. In addition, the authors go on to incorrectly state that at the time of publication vibegron had not been approved by the US Food and Drug Administration (FDA); vibegron 75 mg in fact received approval by the US FDA for the treatment of OAB in adults in December 2020.[2] Vibegron had also received approval in Japan in 2018 for the treatment of OAB in adults with a once-daily dose of 50 mg. In their description of vibegron, Fontaine *et al.* described results from a phase III study in Japanese patients with OAB in which vibegron demonstrated significant improvement in symptoms compared with placebo, as well as fewer adverse events (AEs) compared with imidafenacin.[3] Since the phase III trial in Japan, the international, 12-week phase III EMPOWUR trial and its 40-week extension trial were completed and results published.[4,5] To summarize, in EMPOWUR patients who received vibegron demonstrated significant improvements from baseline in the major symptoms of OAB, including micturitions, urge urinary incontinence episodes, and urgency episodes *versus* placebo ($p < 0.01$, each). The rates of AEs of clinical interest were similar *versus* placebo, including the incidence of hypertension (both 1.7%).[4] Improvements in efficacy endpoints were maintained for patients receiving vibegron for 52 weeks during the extension trial.[5] As such, it was a large oversight to omit the most recent data regarding vibegron from the discussion of OAB management. In Table 1 of their manuscript, the authors present a comparison of the medications available for the management of OAB, which did not include vibegron. Pertinent to the data included in Table 1, once-daily vibegron 75 mg achieves similar efficacy in patients with OAB wet (i.e. with incontinence) and OAB dry (i.e. without incontinence), and 90.4% of patients in the EMPOWUR trials completed the 12-week study. Significantly more patients achieved a ⩾75% reduction in urge urinary incontinence at week 12 with vibegron (49.3%) *versus* placebo (32.8%). The most common AEs occurring at an incidence greater than placebo from the EMPOWUR trial were headache (4.0%) and nasopharyngitis (2.8%).[4]

While a table comparing the available medications, as in Table 1, is helpful, the references cited for the safety data are for a 2012 review and a 2014 systematic literature review[6,7] and do not appear to account for all data presented. I noted possible irregularities. For example, the rate of reported AEs for fesoterodine seems high. Based on phase II and III controlled trials, the incidence of dry mouth was 19% with 4 mg/day and 35% with 8 mg/day.[8] Complete clarity on the data sources and from more recent primary publications would assist in the important comparison of these medications.

The authors noted that precautions should be taken by patients with hypertension when using mirabegron; in addition to this, I think it is important to note that patients taking medications metabolized by CYP2D6 should also be aware that mirabegron is a moderate CYP2D6 inhibitor.[9] Vibegron, however, has no associated hypertension or CYP2D6 drug interaction warnings in the US prescribing information and is a crushable tablet.[2] Vibegron is an efficacious and safe approved treatment option for adults with OAB, a chronic condition prevalent among adults, and

is an important part of the conversation about OAB treatment.

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David Staskin: Conceptualization; Validation; Formal analysis; Supervision; Writing – original draft; Writing – review & editing

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