Critical appraisal of rotigotine transdermal system in management of Parkinson’s disease and restless legs syndrome – patient considerations [Corrigendum]

Kesayan T, Shaw JD, Jones TM, Staffetti JS, Zesiewicz TA. Degenerative Neurological and Neuromuscular Disease 2015;5:63–72.

The authors would like to correct the following errors: on page 64; paragraph 1, “RTG doses for treatment of early-stage PD monotherapy range from 2 mg/24 hours to 6 mg/24 hours, with recommended titration of 2 mg/24 hours weekly.” For adjunct therapy in advanced-stage PD, RTG may be started at 2 mg/24 hour period and titrated up weekly by an additional 2 mg/24 hour period, with a maximum recommended dose of 16 mg/24 hours.” should be “RTG doses for treatment of early-stage PD monotherapy range from 2 mg/24 hours to 8 mg/24 hours (2–6 mg/24 hours in the US), with recommended titration of 2 mg/24 hours weekly. For adjunct therapy in advanced-stage PD, RTG may be started at 4 mg/24 hour period and titrated up weekly by an additional 2 mg/24 hour period, with a maximum recommended dose of 16 mg/24 hours (4–8 mg/24 hours in the US).”

On page 64; paragraph 5, “The mean RTG dose was 8 mg/24 hours, while the mean ropinirole dose was 14.1 mg/day.” should have been “The majority of patients (92%) received RTG maintenance dose of 8 mg/24 h, while the median ropinirole dose was 14.1 mg/day.”

On page 64; paragraph 6, “Three hundred and forty-one patients were randomized to receive RTG 8 mg/24 hours, 12 mg/24 hours, or placebo for 28 weeks.” should have been “Three hundred and forty-one patients were randomized to receive RTG up to 8 mg/24 hours, up to 12 mg/24 hours, or placebo for 28 weeks.”

On page 65; Table 1, data in the Doses column and the Notes section have been updated.

Table 1 Efficacy of RTG in early and advanced PD

| Dose (mg/24 hour) | n  | Change from baseline ± SD (P-value) | UPDRS II ADL | UPDRS III motor |
|-------------------|----|----------------------------------|-------------|----------------|
| **Early PD**      |    |                                   |             |                |
| Güldenpfneg et al10 | 8 mg/24 hour | 25  | -2.84±3.45 (0.0004) | -4.88±5.56 (0.0002) |
| <8 mg/24 hour     | 4  | -2.25±3.36 (0.1622)               |             |                |
| Plo               | 0  | -                                |             |                |
| Jankovic et al11  | 5.7 mg/24 hour | 177 | -0.19±0.26 (0.002)  | -3.58±0.54 (0.001) |
| Plo               | 96 | 0.92±0.35 (0.002)                | 0.38±0.73 (0.001) |
| Parkinson Study Group22 | 2 mg/24 hour | 49  | -0.04(0.94)         | -0.90(0.44)  |
| 4 mg/24 hour      | 47 | -0.04(0.11)                      | -1.88(0.11) |
| 6 mg/24 hour      | 48 | -0.92(0.08)                      | -3.91(0.001) |
| 8 mg/24 hour      | 51 | -1.56(0.003)                     | -3.82(0.001) |
| Plo               | 47 | -                                | -            |
| Watts et al12     | 5.7 mg* | 180 | -0.30±3.54           | -3.50±7.26  |
| Plo               | 96 | -                                | -            |
| Giladi et al2     | 8 mgc | 215 | -2.1d              | -5.2c        |
| Plo               | 118 | -0.1                              | -2.1          |
| Trenkwalder et al13 | 2–16 mg | 178 | -2.6±3.6            | -7.0(0.002)  |
| Plo               | 89  | -1.3±3.4                         | -3.9          |
| **Advanced PD**   |    |                                   |             |                |
| LeWitt et al16    | ≤8 mg/24 h | 113 | -3.1(0.004)         | -6.8(0.0185) |
|                   | ≤12 mg/24 h | 109  | -3.2(0.0023)        | -8.7(0.0006) |
|                   | Plo       | 119  | -0.5               | -3.4          |

(Continued)
On page 66; paragraph 2, “In an open-label study, advanced-PD patients were treated with levodopa, pramipexole (<1.5 mg/day), or ropinirole (<6.0 mg/day), and RTG (<8 mg/24 hours) for an 8-week treatment period.”

On page 68; Table 3, data in the Study, doses column for the Stiasny-Kolster study and the Notes section have been updated.
On page 69; Table 4, the data for the Stiasny–Kolster study and the Notes section have been updated.

### Table 4 Side effects present in participants (%) during randomized, double–blinded, placebo–controlled trials

| Side effect         | Dose (mg/24 hour) | Inoue et al. | Hening et al. | Trenkwalder et al. | Oertel et al. | Oertel et al. | Stiasny–Kolstera,b |
|---------------------|-------------------|--------------|---------------|--------------------|---------------|---------------|-------------------|
|                     | RTG   | Plo   | RTG   | Plo   | RTG   | Plo   | RTG   | Plo   | RTG   | Plo   | RTG   | Plo   |
| Application         | 0.5 mg  | 7.4   | 22.2  | 5.0   | 9.8   | 1.8   | 4.8   | 17.6  | 28.6  |
| site reaction       | 1 mg    | -     | 17    | -     | 35.0  | 2.0   | 15.6  | -     | 38.5  |
|                     | 2 mg    | 42.1  | 34.3  | 41.0  | 16.3  | 17.4  | 26.3  | -     | -     |
|                     | 3 mg    | 50.0  | 34    | 52.0  | 20    | -     | -     | -     | -     |
|                     | 4 mg    | -     | -     | -     | 25    | -     | -     | -     | -     |
| Headache            | 0.5 mg  | 0     | 14.1  | 8.0   | 11.8  | 7.3   | 14.3  | 11.8  | 7.1   |
|                     | 1 mg    | -     | 12    | -     | 10.0  | 7.0   | 7.8   | -     | 38.5  |
|                     | 2 mg    | 5.3   | 10.1  | 13.0  | 2     | -     | 17.4  | 21.1  | -     |
|                     | 3 mg    | 2.1   | 10.4  | 16.0  | 4.6   | -     | -     | -     | -     |
|                     | 4 mg    | -     | -     | -     | 12.5  | -     | -     | -     | -     |
| Nausea              | 0.5 mg  | 9.5   | 13.1  | 10.0  | 5.9   | 9.1   | 4.8   | 0.0   | 14.3  |
|                     | 1 mg    | -     | 20    | 9.0   | 9.4   | -     | -     | 7.7   | -     |
|                     | 2 mg    | 3.3   | 18.2  | 21.0  | 6.1   | -     | 21.7  | 5.3   | -     |
|                     | 3 mg    | 43.6  | 20.8  | 18.0  | 24.6  | -     | -     | -     | -     |
|                     | 4 mg    | -     | -     | -     | 23.2  | -     | -     | -     | -     |
| Fatigue             | 0.5 mg  | -     | 10.1  | 4.0   | 3.9   | 9.1   | 9.5   | 0.0   | 0.0   |
|                     | 1 mg    | -     | 3     | 7.0   | 9.0   | 4.7   | -     | -     | 0.0   |
|                     | 2 mg    | -     | 7.1   | 15.0  | 6.1   | -     | 8.7   | 10.5  | -     |
|                     | 3 mg    | -     | 6.6   | 11.0  | 10.8  | -     | -     | -     | -     |
|                     | 4 mg    | -     | -     | -     | 7.1   | -     | -     | -     | -     |
| Pruritus            | 0.5 mg  | -     | 9.1   | 2.0   | 5.9   | 1.8   | -     | 5.9   | 7.1   |
|                     | 1 mg    | -     | 2     | -     | 3.1   | -     | -     | 15.4  | -     |
|                     | 2 mg    | -     | 3     | -     | 0     | -     | -     | 0.0   | -     |
|                     | 3 mg    | -     | 7.5   | -     | 10.8  | -     | -     | -     | -     |
|                     | 4 mg    | -     | -     | -     | 3.6   | -     | -     | -     | -     |
| Hyperhidrosis       | 0.5 mg  | -     | -     | -     | -     | -     | -     | -     | 0.0   |
|                     | 1 mg    | -     | -     | -     | 5.0   | 3.0   | -     | -     | -     |
|                     | 2 mg    | -     | -     | -     | 6.0   | -     | -     | -     | -     |
|                     | 3 mg    | -     | -     | -     | 4.0   | -     | -     | -     | 10.5  |
|                     | 4 mg    | -     | -     | -     | -     | -     | -     | -     | -     |
| Somnolence          | 0.5 mg  | 2.1   | 8.1   | 6.0   | -     | -     | -     | 9.5   | -     |
|                     | 1 mg    | -     | 10.0  | -     | -     | -     | -     | -     | -     |
|                     | 2 mg    | 10.5  | 13.1  | -     | -     | -     | 10.9  | -     | -     |
|                     | 3 mg    | -     | 15.1  | -     | -     | -     | -     | -     | -     |
|                     | 4 mg    | -     | -     | -     | -     | -     | -     | -     | -     |

Notes: The study did not report the association of adverse events (AE) in relation to the dose of RTG. A mean dose of RTG in the treatment group was reported as 2.1 mg/24 hours; RTG content per system (mg) originally reported; RTG nominal doses (mg/24 h) were calculated using a ratio of 2.25 (as per US prescribing information), i.e., 1.125 mg is equivalent to 0.5 mg/24 h, 2.25 mg to 1 mg/24 h, and 4.5 mg to 2 mg/24 h.

Abbreviations: RTG, rotigotine; Plo, placebo.