


Correction to: Clinical Pharmacokinetic Characteristics of Cebranopadol, a Novel First-in-Class Analgesic

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Correction to: Clin Pharmacokinet (2018) 57:31–50
<https://doi.org/10.1007/s40262-017-0545-1>

Page 40, column 2, para 1 which reads as

For each simulation, PK profiles from 1000 subjects were simulated based on a titration scheme of 100 µg for 6 days, 200 µg for 6 days and 400 µg for 6 days to reach the cebranopadol target dose of 600 µg. Median values of maximum concentration at steady state ($C_{\max,ss}$) and area under the curve at steady state (AUC_{ss}) were calculated. The time to reach steady state was calculated as the time point when the AUC reaches 98% of the AUC at absolute steady state, e.g. maximum AUC value during a duration of 50 days.

should read

For each deterministic simulation (i.e., the interindividual variability was fixed to 0), one subject PK profile was simulated based on an optimized titration scheme to reach the cebranopadol target dose of 600 µg (100 µg of 6 days, 200 µg of 6 days, 400 µg of 6 days and 600 µg). The steady-state was defined to be achieved on Day 40 in the

simulation to calculate the values of maximum concentration at steady state ($C_{\max,ss}$) and area under the curve at steady state ($AUC_{t,ss}$) as reported in Table 14.

Page 45, column 2, para 4 which reads as

As shown in Table 14, the impact of age and body weight on $C_{\max,ss}$ and AUC_{ss} was lower than 3% with respect to the values of the typical patient considered as reference, whereas the impact of lower CrCl values accounted for increases in $C_{\max,ss}$ and AUC_{ss} up to 30 and 34% in the investigated range, respectively. Females had 13% higher $C_{\max,ss}$ and 17% higher AUC_{ss} than males due to the fact that sex significantly correlated with clearance (Table 14). As the histogram in Fig. 4 shows, a considerable overlap exists between the distributions of male and female clearances.

should read

As shown in Table 14, the impact of age and body weight on $C_{\max,ss}$ and AUC_{ss} was lower or equal to 1% with respect to the values of the typical patient considered as reference, whereas the impact of lower CrCl values accounted for increases in $C_{\max,ss}$ and AUC_{ss} up to 28 and 34% in the investigated range, respectively. Females had 14% higher $C_{\max,ss}$ and 17% higher AUC_{ss} than males due to the fact that sex significantly correlated with clearance (Table 14). As the histogram in Fig. 4 shows, a considerable overlap exists between the distributions of male and female clearances.

Page 45, column 2, para 5 and page 46, column 1, para 1 which read as

The simulations also indicated that low back pain/osteoarthritis and diabetic polyneuropathy patient populations can have up to 29.5% higher $C_{\max,ss}$ and AUC_{ss} values compared with healthy subjects (Table 14).

The original article can be found online at <https://doi.org/10.1007/s40262-017-0545-1>.

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should read

The simulations also indicated that low back pain/osteoarthritis, bunionectomy and diabetic polyneuropathy patient populations can have 19–114% higher $C_{max,ss}$ and AUC_{ss} values compared with healthy subjects (Table 14).

Page 46, Table 13, column 1, rows 27 and 28 which read as

Bunionectomy patients
DPN patients

should read

DPN patients
Bunionectomy patients

Page 48, Table 14 should appear as

Covariate	$C_{max,ss}$ (pg/mL)	% Change in $C_{max,ss}$	$AUC_{\tau,ss}$ (pg h/mL)	% Change in $AUC_{\tau,ss}$
Reference values	378	0	6790	0
Female sex	432	14	7960	17
Age (years)				
40	375	– 1	6790	0
60	379	0	6790	0
75	381	1	6790	0
CrCl (mL/min)				
45	483	28	9080	34
60	446	18	8250	21
80	410	9	7480	10
Body weight (kg)				
70	379	0	6810	0
100	377	0	6760	– 1
120	375	– 1	6720	– 1
Disease status				
Healthy	316	– 16	5690	– 16
DPN	428	13	7690	13
Bunionectomy patients	681	80	12200	80

The titration scheme to reach cebranopadol 600 μ g is defined as cebranopadol 100 μ g for 6 days, cebranopadol 200 μ g for 6 days, cebranopadol 400 μ g for 6 days and cebranopadol 600 μ g

The reference values for the covariates, defined as the median values for continuous covariates and the most frequent category for categorical covariates, except disease status, were: sex = male, formulation = tablet, CYP2C9 status = unknown, disease status = LBP and OA patients, age (years) = 55, CrCl (mL/min) = 106.4, body weight (kg) = 82, ALT (units/L) = 19

ALT alanine transferase, $AUC_{\tau,ss}$ area under the plasma concentration-time curve for one 24 h dosing interval at steady state, $C_{max,ss}$ maximum plasma concentration at steady state, CrCl creatinine clearance, CYP cytochrome P450, DPN diabetic polyneuropathy, LBP low back pain, OA osteoarthritis

Page 49, column 2, para 2, lines 4–5 which read as
...exceed an overall 35% change in cebranopadol exposure in the investigated dose range.

should read

...exceed an overall 35% change in cebranopadol exposure in the investigated dose range except for bunionectomy patients.

Page 49, column 2, para 4, lines 2–3 which read as
...cebranopadol is comparable in healthy subjects and patients.

should read

...cebranopadol is comparable in healthy subjects and in patients with chronic pain.

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