

Corrigendum: Population Pharmacokinetics of S(-)-Carvedilol in Healthy Volunteers After Administration of the Immediate-Release (IR) and the New Controlled-Release (CR) Dosage Forms of the Racemate

Received: June 25, 2007; Accepted: June 25, 2007; Published: September 28, 2007

Ahmed A. Othman,¹ David M. Tenero,² Duane A. Boyle,² Natalie D. Eddington,¹ and Michael J. Fossler²

AAPS Journal. 2007;9(2):E208-E218. DOI: 10.1208/aapsj0902023

The author affiliation for Natalie D. Eddington was omitted and should have been affiliation 1.

The first paragraph, fifth sentence of the Introduction was incorrect. The sentence should have read: The *S*(-) enantiomer is primarily responsible for the β -blocking effect of carvedilol, whereas both the *R*(+) and *S*(-)enantiomers contribute to the α_1 -blockade.^{7,8}

The data alignment in Table 1 was presented incorrectly and should have been:

The data and data alignment in Table 3 was presented incorrectly and should have been:

The data alignment in Table 4 was presented incorrectly and should have been:

Table 1. Final Population Parameter Estimates for Analysis of the PK Data for the Controlled Release (CR) and Immediate Release (IR) Dosage Forms of Carvedilol

Parameter		Point Estimate (% RSE)	% ISV ^a (% RSE)	% IOV ^b (% RSE)
CL/F (L/hr)		149 (4.8)		
Vc/F (L)		828 (6.6)	37.1 (15.6)	
Vp/F (L)		1150 (10.3)		
Q/F (L/hr)		94.7 (5.3)		
KA (hr ⁻¹)	CR	0-2 hr 0.08 (16.0) 2-4 hr 0.27 (16.1) > 4 hr 3.5 (17.7)		
	IR _{AM}	0-1 hr 0.92 (21.5) > 1 hr 8.79 (42.1)	94.6 (33.0)	113.6 (24.1)
	IR _{PM}	0-1 hr 0.42 (26.7) > 1hr 3.0 (31.9)	140.4 (20.4)	193.1 (17.8)
F _{rel}	CR	0.76 (7.4)		
	IR _{AM}	1 (Fixed)	33.8 (14.1)	14.1 (67.3)
	IR _{PM}	0.80 (3.2)		
Tlag (h)	CR	0.23 (Fixed)		
	IR	0.2 (5.3)		
σ^2 (Residual Error)		0.10 (5.8)	21.95 (27.4)	

Table 3. Evaluation of the Final Model by Leverage Analysis

Parameter	Mean of 10 Leverage Analysis Runs (% CV)	Final Model Point Estimate
$\theta_{CL/F}$ (L/hr)	149 (2.5)	149
$\theta_{Vc/F}$ (L)	828 (4.8)	828
$\theta_{Vp/F}$ (L)	1147 (5.9)	1150
$\theta_{Q/F}$ (L/hr)	95 (2.9)	94.7
$\theta_{KA,CR}$ 0-2 hr (hr ⁻¹)	0.09 (11.8)	0.08
$\theta_{KA,CR}$ 2-4 hr (hr ⁻¹)	0.29 (9.6)	0.27
$\theta_{KA,CR} > 4$ hr (hr ⁻¹)	3.83 (7.0)	3.50
$\theta_{KA,IR,AM}$ 0-1 hr (hr ⁻¹)	0.92 (14.7)	0.92
$\theta_{KA,IR,AM} > 1$ hr (hr ⁻¹)	8.40 (37.3)	8.79
$\theta_{KA,IR,PM}$ 0-1 hr (hr ⁻¹)	0.42 (14.3)	0.42
$\theta_{KA,IR,PM} > 1$ hr (hr ⁻¹)	3.03 (15.1)	3.0
$\theta_{Frel,CR}$	0.76 (5.9)	0.76
$\theta_{Frel,IR,AM}$	1 (Fixed)	1 (Fixed)
$\theta_{Frel,IR,PM}$	0.80 (1.9)	0.80
$\theta_{Tlag,CR}$ (hr)	0.23 (Fixed)	0.23 (Fixed)
$\theta_{Tlag,IR}$ (hr)	0.20 (4.0)	0.20
$\omega_{Vc / F}$ 2	0.14 (6.6)	0.14
$\omega_{KA,CR}$ 2	0.98 (15.5)	0.90
$\omega_{KA,IR,AM}$ 2	2.05 (12.2)	1.97
$\omega_{KA,IR,PM}$ 2	3.81 (12.7)	3.73
ω_{Frel} 2	0.12 (5.9)	0.11
$\omega_{RES\ ERR}$ 2	0.05 (14.8)	0.05
$\pi_{KA,CR}$ 2	1.47 (15.4)	1.29
$\pi_{Frel,CR}$ 2	0.015 (41.3)	0.02
σ^2	0.10 (3.1)	0.10

Table 4. Evaluation of the Final Model by Simulation

Parameter	CR Dosage Form				IR Dosage Form	
	10 mg	20 mg	40 mg	80 mg	25 mg (am)	25 mg (pm)
AUC _{0-tlast} (ng*h/mL) ^a	Observed median	12.75	31.77	71.29	145.59	59.65
C _{max} (ng/mL)	90% prediction interval ^c	11.66-21.74	27.65-48.67	57.80-98.50	116.73-193.73	48.80-61.39
	Observed median	1.81	3.76	8.13	17.87	15.65
T _{max} (h)	90% Prediction interval	1.80-3.22	3.52-6.53	6.99-13.23	14.02-25.75	11.62-15.03
	Observed median	6	5	5	5	1.5
C _{min} (ng/mL) ^b	90% Prediction interval	4-6	4.5-6	4.5-6	4.5-6	1.5-2
	Observed median	0.29	0.41	0.93	1.81	1.49
	90% Prediction interval	0.23-0.40	0.31-0.59	0.57-1.11	1.11-2.12	1.32-1.75
						1.78-2.38