

Electronic Supplementary Material

**Effectiveness and Tolerability of Tapentadol Prolonged Release Compared With
Prior Opioid Therapy for the Management of Severe, Chronic Osteoarthritis Pain**

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**Table S1. Responder Rates 1 and 2 at Baseline and at Weeks 6 and 12 Using Observed-case Analysis
(With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF
(Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population**

	Observed-case analysis			LOCF	
	Week 6	Week 12		Week 6	Week 12
		With Substudy A (n=55)	Without Substudy A (n=33)		Without Substudy A (n=41)
Responder rate, n (%)					
Responder rate 1	51 (92.7) ^a	53 (98.1) ^a	32 (97.0) ^a	54 (87.1) ^a	36 (87.8) ^a
Responder rate 2	49 (89.1) ^a	50 (92.6) ^a	30 (90.9) ^a	50 (80.6) ^a	32 (78.0) ^a

LOCF, last observation carried forward.

^a $P < 0.001$ for testing the hypothesis that the response is 50%.

Table S2. Mean (SD) Pain Intensity Scores (NRS-3) at Baseline and at Weeks 6 and 12 Using Observed-case Analysis (With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF (Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population

		Observed-case analysis			LOCF	
	Baseline	Week 6	Week 12		Week 6	Week 12
		With Substudy A	Without Substudy A		Without Substudy A	
Pain intensity	(n=62)	(n=55)	(n=53)	(n=32)	(n=62)	(n=41)
Mean (SD) pain intensity	4.7 (0.66)	2.5 (1.46) ^a	1.8 (1.41) ^a	2.2 (1.11) ^a	2.9 (1.94) ^a	2.9 (2.03) ^a

SD, standard deviation; NRS-3, numerical rating scale-3; LOCF, last observation carried forward.

^a $P < 0.0001$ for the change from baseline.

Table S3. Subject Satisfaction With Treatment Ratings at Baseline and at Weeks 6 and 12 Using Observed-case Analysis (With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF (Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population

		Observed-case analysis			LOCF	
	Baseline	Week 6	Week 12		Week 6	Week 12
Satisfaction rating, n (%)	(n=62)	With Substudy A (n=55)	Without Substudy A (n=54)	Without Substudy A (n=33)	Without Substudy A (n=62)	Without Substudy A (n=41)
Excellent	0	3 (5.5)	15 (27.8)	3 (9.1)	3 (4.8)	3 (7.3)
Very good	0	27 (49.1)	18 (33.3)	16 (48.5)	28 (45.2)	18 (43.9)
Good	1 (1.6)	21 (38.2)	18 (33.3)	12 (36.4)	22 (35.5)	13 (31.7)
Fair	46 (74.2)	4 (7.3)	2 (3.7)	1 (3.0)	6 (9.7)	4 (9.8)
Poor	15 (24.2)	0	0	0	3 (4.8)	3 (7.3)
Missing	0	0	1 (1.9)	1 (3.0)	0	0

LOCF, last observation carried forward.

Table S4. PGIC and CGIC Ratings at Baseline and at Weeks 6 and 12 Using Observed-case Analysis (With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF (Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population

	Observed-case analysis			LOCF	
	Week 6	Week 12		Week 6	Week 12
		With Substudy A	Without Substudy A		Without Substudy A
Rating, n (%)	(n=55)	(n=54)	(n=33)	(n=62)	(n=41)
<i>PGIC</i>					
Very much improved	6 (10.9)	15 (27.8)	3 (9.1)	6 (9.7)	3 (7.3)
Much improved	28 (50.9)	21 (38.9)	17 (51.5)	28 (45.2)	18 (43.9)
Minimally improved	18 (32.7)	14 (25.9)	11 (33.3)	20 (32.3)	14 (34.1)
No change	1 (1.8)	2 (3.7)	1 (3.0)	2 (3.2)	2 (4.9)
Minimally worse	2 (3.6)	0	0	3 (4.8)	1 (2.4)
Much worse	0	1 (1.9)	0	2 (3.2)	2 (4.9)
Very much worse	0	0	0	1 (1.6)	1 (2.4)
Missing	0	1 (1.9)	1 (3.0)	0	0
<i>CGIC</i>					
Very much improved	6 (10.9)	15 (27.8)	3 (9.1)	6 (9.7)	3 (7.3)
Much improved	28 (50.9)	21 (38.9)	17 (51.5)	28 (45.2)	18 (43.9)
Minimally improved	18 (32.7)	15 (27.8)	11 (33.3)	20 (32.3)	14 (34.1)
No change	1 (1.8)	2 (3.7)	1 (3.0)	1 (1.6)	1 (2.4)
Minimally worse	2 (3.6)	0	0	4 (6.5)	2 (4.9)
Much worse	0	0	0	1 (1.6)	1 (2.4)
Very much worse	0	0	0	2 (3.2)	2 (4.9)
Missing	0	1 (1.9)	1 (3.0)	0	0

PGIC, patient global impression of change; CGIC, clinician global impression of change; LOCF, last observation carried forward.

Table S5. Mean (SD) WOMAC Scores at Baseline and at Weeks 6 and 12 Using Observed-case Analysis (With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF (Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population

		Observed-case analysis			LOCF	
	Baseline	Week 6	Week 12		Week 6	Week 12
		With	Without			
		Substudy A	Substudy A			
WOMAC score	(n=62)	(n=55)	(n=53)	(n=32)	(n=61)	(n=40)
Global score ^a	54.2 (13.19)	29.5 (16.72) ^b	21.6 (19.00) ^b	24.8 (17.00) ^b	32.7 (19.26) ^b	31.8 (21.86) ^b
Pain subscale ^c	11.0 (2.48)	5.7 (3.45) ^b	4.1 (3.59) ^b	5.0 (3.49) ^b	6.4 (4.00) ^b	6.4 (4.47) ^b
Stiffness subscale ^d	4.4 (1.76)	2.7 (1.52) ^b	1.8 (1.78) ^b	2.1 (1.58) ^b	2.9 (1.67) ^b	2.7 (1.91) ^e
Physical function subscale ^f	38.9 (9.88)	21.2 (12.40) ^b	15.6 (14.04) ^b	17.7 (12.36) ^b	23.4 (14.23) ^b	22.7 (15.94) ^b

WOMAC, Western Ontario and McMaster Universities; LOCF, last observation carried forward.

^aPossible score, 0 to 96.

^b $P < 0.0001$ for the change from baseline.

^cPossible score, 0 to 20.

^dPossible score, 0 to 8.

^e $P = 0.0005$ for the change from baseline.

^fPossible score, 0 to 68.

Table S6. Mean (SD) EQ-5D Scores at Baseline and at Weeks 6 and 12 Using Observed-case Analysis (With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF (Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population

		Observed-case analysis			LOCF	
	Baseline	Week 6	Week 12		Week 6	Week 12
		With	Without		Without	
		Substudy A	Substudy A		Substudy A	
EQ-5D score	(n=62)	(n=55)	(n=53)	(n=32)	(n=60)	(n=39)
Health status index score	0.5 (0.30)	0.7 (0.18) ^a	0.8 (0.23) ^a	0.7 (0.24) ^b	0.7 (0.22) ^a	0.6 (0.30) ^b
Patient's health state assessment (100-mm VAS)	47.8 (15.91)	76.1 (17.66) ^a	82.6 (17.30) ^a	81.1 (15.21) ^a	73.9 (20.57) ^a	75.9 (22.11) ^a

SD, standard deviation; EQ-5D, EuroQol-5 Dimension; LOCF, last observation carried forward; VAS, visual analog scale.

^a $P < 0.0001$ for the change from baseline.

^b $P < 0.01$ for the change from baseline.

**Table S7. Mean (SD) SF-36 Scores at Baseline and at Weeks 6 and 12 Using Observed-case Analysis
(With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF
(Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population**

		Observed-case analysis			LOCF	
	Baseline	Week 6	Week 12		Week 6	Week 12
			With	Without		
			Substudy A	Substudy A		Without
Subscale or summary	(n=62)	(n=55)	(n=53)	(n=32)	(n=60)	Substudy A (n=39)
Role-physical	33.1 (43.60)	61.8 (43.26) ^a	72.6 (41.97) ^a	76.6 (41.61) ^b	60.0 (44.20) ^a	70.5 (45.11) ^b
Physical functioning	35.9 (22.19)	62.1 (24.55) ^a	69.8 (27.01) ^a	68.8 (22.36) ^a	59.8 (26.13) ^a	63.5 (26.21) ^a
Bodily pain	32.5 (12.32)	54.8 (16.62) ^a	63.2 (23.71) ^a	55.0 (16.33) ^a	52.1 (18.71) ^a	50.2 (19.71) ^a
General health	51.1 (17.85)	64.7 (20.83) ^a	67.4 (22.66) ^a	60.7 (17.44) ^a	63.2 (21.14) ^a	58.3 (18.89) ^a
Vitality ^c	46.1 (21.16)	58.0 (25.40) ^a	61.0 (25.71) ^a	54.7 (16.58) ^a	56.1 (25.81) ^a	50.8 (18.55) ^b
Social functioning	66.1 (27.85)	82.0 (25.66) ^a	84.0 (23.94) ^a	86.3 (21.85) ^b	81.7 (26.39) ^a	84.9 (23.68) ^b
Role-emotional	74.7 (42.11)	75.8 (39.78)	77.4 (39.10)	81.3 (35.86)	74.4 (40.88)	77.8 (38.49)
Mental health ^c	69.7 (22.90)	76.5 (22.08) ^a	78.9 (21.69) ^a	77.4 (19.17) ^b	74.6 (23.87) ^b	72.6 (23.15)
Physical component	28.4 (8.97)	40.2 (8.84) ^a	43.9 (10.72) ^a	42.0 (8.68) ^a	39.3 (9.47) ^a	40.1 (10.09) ^a
Mental component	52.6 (12.85)	53.1 (12.54)	52.9 (11.28)	53.0 (10.04)	52.5 (13.05)	52.0 (11.23)

SD, standard deviation; SF-36; Short Form-36; LOCF, last observation carried forward.

^a $P \leq 0.0005$ for the change from baseline.

^b $P < 0.05$ for the change from baseline.

^cBaseline, n=62; Observed-case analysis: Week 6, n =55; Week 12 (with Substudy A), n=52; Week 12 (without Substudy A), n=31; LOCF: Week 6, n=60; Week 12 (without Substudy A), n=39.

Table S8. Mean (SD) HADS Anxiety and Depression Subscale Scores at Baseline and at Weeks 6 and 12 Using Observed-case Analysis (With and Without the Week 9-12 Data for the Substudy A Population) and Using the LOCF (Without the Week 9-12 Data for the Substudy A Population) – Main Analysis Population

		Observed-case analysis			LOCF	
	Baseline	Week 6	Week 12		Week 6	Week 12
			With	Without		Without
			Substudy A	Substudy A		Substudy A
Subscale	(n=61)	(n=55)	(n=53)	(n=32)	(n=60)	(n=39)
Anxiety subscale	5.2 (4.26)	4.0 (4.07) ^a	3.5 (3.74) ^a	4.0 (3.65) ^a	4.3 (4.34)	4.7 (4.12)
Depression subscale	5.1 (4.64)	4.1 (4.08) ^a	3.7 (4.04) ^a	3.8 (3.48) ^a	4.4 (4.55)	4.6 (4.63)

SD, standard deviation; HADS, Hospital Anxiety and Depression Scale; LOCF, last observation carried forward.

^a $P < 0.05$ for the change from baseline.

Table S9. Sleep Questionnaire Scores: A) Mean (SD) Time to Fall Asleep, Time Slept, and Number of Awakenings at Night and B) Sleep Quality Using Observed-case Analysis (With and Without the Substudy A Population) and Using the LOCF (Without the Substudy A Population) – Main Analysis Population

A) Time to fall asleep, time slept, and number of awakenings

		Observed-case analysis			LOCF	
Baseline		Week 6	Week 12		Week 6	Week 12
			With Substudy A	Without Substudy A		Without Substudy A
Mean (SD) sleep measure	(n=62)	(n=55)	(n=52)	(n=31)	(n=60)	(n=39)
Time to fall asleep, hours	0.6 (0.52)	0.5 (0.62)	0.5 (0.59)	0.5 (0.54)	0.5 (0.62)	0.5 (0.53)
Time slept, hours	6.6 (1.38)	7.0 (1.09) ^a	7.0 (1.18) ^a	7.1 (1.18)	7.0 (1.09) ^a	7.2 (1.28)
Number of awakenings	2.3 (1.54)	1.1 (1.12) ^b	1.1 (1.06) ^b	1.4 (0.92)	1.3 (1.27) ^b	1.6 (1.18)

A) Sleep quality

		Observed-case analysis			LOCF	
Baseline		Week 6	Week 12		Week 6	Week 12
			With Substudy A	Without Substudy A		Without Substudy A
Sleep quality, n (%)	(n=62)	(n=55)	(n=54)	(n=33)	(n=60)	(n=39)
Excellent	2 (3.2)	12 (21.8)	16 (29.6)	4 (12.1)	12 (20.0)	4 (10.3)
Good	21 (33.9)	23 (41.8)	21 (38.9)	14 (42.4)	25 (41.7)	17 (43.6)
Fair	20 (32.3)	17 (30.9)	14 (25.9)	12 (36.4)	19 (31.7)	16 (41.0)
Poor	19 (30.6)	3 (5.5)	1 (1.9)	1 (3.0)	4 (6.7)	2 (5.1)
Missing	0	0	2 (3.7)	2 (6.1)	0	0

SD, standard deviation; LOCF, last observation carried forward.

^a $P < 0.05$ for the change from baseline.

^b $P < 0.0001$ for the change from baseline.