5.2. Tabular Listing of All Clinical Studies

Cymbalta (duloxetine hydrochloride) Diabetic Neuropathic Pain

Date approved by Lilly: 17 February 2004

Lilly Research Laboratories Eli Lilly and Company Indianapolis, Indiana, USA

Table 5.2.

Tabular Listing of Clinical Studies

Study Identifier; Location;		Enrollment Start		Test and Control Drug(s)	# Patients (M/F)	Diagnosis or		
Status;		Status and	Design;	Dose, Route,	Mean Age	Inclusion	Treatment	Primary
Report Type	Objective(s)	End	Control Type	and Regimen	(Range) years	Criteria	Duration	Endpoint
F1J-MC-	Safety and	February 1999	Multicenter,	Duloxetine	N = 173	DSM-IV-	8 weeks	HAMD ₁₇
HMAQ(a);	Efficacy	Complete	parallel group,	capsules: 10 mg,	(M = 62;	defined MDD		Total
5.3.5.4.1		May 2000	double-blind,	20 mg	F = 111	(current		Score
(5.3.5.1.2.1);			randomized	Fluoxetine		episode		
Complete;			placebo-controlled,	capsules: 20 mg	41.4 years	duration ≥2		
Full			blinded placebo	Placebo capsules	(18.7-65)	weeks); CG1-		
			lead-in and lead-			Severity		
			out	Duloxetine:		Score ≥4;		
				20-60 mg		clinician-rated		
				PO BID		HAMD ₁₇ total		
				Fluoxetine: 20		score ≥15 at	***************************************	
		-		mg PO QD		Visits 1 and 2	-	
				Placebo				

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-	Safety and	March 1999	Multicenter,	Duloxetine	N = 194	DSM-IV-	8 weeks	HAMD ₁₇
HMAQ(b);	Efficacy	Complete	parallel group,	capsules: 10 mg,	(M = 65;	defined MDD		Total
5.3.5.4.1		January 2001	double-blind,	20 mg	F = 129)	(current		Score
(5.3.5.1.2.2);			randomized	Fluoxetine		episode		
Complete;			placebo-controlled,	capsules: 20 mg	40.4 years	duration ≥2		
Full			blinded placebo	Placebo capsules	(18.9-64.4)	weeks); CGI-		
			lead-in and lead-			Severity		
			out	Duloxetine:		score ≥4;		
				20-60 mg		clinician-rated		
				PO BID		HAMD ₁₇ total		***
				Fluoxetine: 20		score ≥15 at		
				mg PO QD	-	Visits 1 and 2		
				Placebo				

Table 5.2. Tabul

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-	Safety and	March 2000	Multicenter,	Duloxetine	N = 353	DSM-IV-	8 weeks	HAMD ₁₇
HMATb;	Efficacy	Complete	parallel, double-	capsules: 20 mg	(M = 136;	defined MDD;		Total
5.3.5.4.1		February 2001	blind, randomized,	Paroxetine	F=217)	CGI-Severity		Score
(5.3.5.1.1.1);			placebo- and active	capsules: 20 mg	40.5	score ≥4 at		
Complete;			comparator-	Placebo capsules	40.5 years	Visits 1 and 2;		
Full			controlled study	D-1	(18.2-78.2)	clinician-rated		
			with blinded	Duloxetine: 20		HAMD ₁₇ total score ≥15 at		
			placebo lead-in and	mg or 40 mg PO BID		Visits 1 and 2		
			pracebo read-out	Paroxetine: 20		Visits I and 2		
				mg PO QD				
Ŧ				Placebo				
F1J-MC-	Safety and	March 2000	Multicenter,	Duloxetine	N = 354	DSM-IV-	8 weeks	HAMD ₁₇
НМАТа;	Efficacy	Complete	parallel, double-	capsules: 20 mg	(M = 136;	defined MDD;		Total
5.3.5.4.1		April 2001	blind, randomized,	Paroxetine	F = 218)	CGI-Severity		Score
(5.3.5.1.1.2);		-	placebo- and active	capsules: 20 mg		score ≥4 at		
Complete;			comparator-	Placebo capsules	43.7 years	Visits 1 and 2;		
Full			controlled study		(18.0-82.2)	clinician-rated		
			with blinded	Duloxetine: 20		HAMD ₁₇ total		
			placebo lead-in and	mg or 40 mg		score ≥15 at		
			placebo lead-out	PO BID		Visits 1 and 2		
				Paroxetine: 20				
				mg PO QD				
				Placebo			<u> </u>	

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
FlJ-MC-	Safety and	November	Multicenter,	Duloxetine	N = 367	DSM-IV-	34 weeks	HAMD ₁₇
HMAYa	Efficacy	2000	parallel, double-	capsules: 20 mg	(M = 100;	defined MDD;		Total
5.3.5.4.1;		Complete	blind, randomized,	Paroxetine	F =267)	CGI-Severity score ≥4 at		Score
(5.3.5.1.1.3);		July 2002	placebo- and active comparator-	capsules: 20 mg Placebo capsules	43.4 years	Visits 1 and 2;		
Complete; Full			controlled study	Tracebo capsures	(19.3-74.4)	clinician-rated		
Tun			with blinded	Duloxetine:	(15.5 / 1.1)	HAMD ₁₇ total		
			placebo lead-in and	40 or 60 mg		score ≥15 at		
			placebo lead out	PO BID		Visits 1 and 2		
				Paroxetine: 20				
				mg PO QD				
				Placebo				
F1J-MC-	Safety and	October 2000	Multicenter,	Duloxetine	N = 392	DSM-IV-	34 weeks	HAMD ₁₇
HMAYb	Efficacy	Complete	parallel, double-	capsules: 20 mg	(M = 119;	defined MDD;		Total
5.3.5.4.1;		July 2002	blind, randomized,	Paroxetine	F = 273	CGI-Severity		Score
(5.3.5.1.1.4);			placebo- and active	capsules: 20 mg		score ≥4 at	***************************************	
Complete;			comparator-	Placebo capsules	45.2 years	Visits 1 and 2;	V-1	
Full			controlled study	D. I.	(20.1-76.7)	clinician-rated		
			with blinded	Duloxetine:		HAMD ₁₇ total		
			placebo lead-in and placebo lead out	40 or 60 mg PO BID		score ≥15 at Visits 1 and 2		
			pracebo lead out	Paroxetine: 20		VISITS I and 2		
				mg PO QD			Value of the state	
				Placebo				

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- HMBHa; 5.3.5.4.1 (5.3.5.1.2.3); Complete; Full	Safety and Efficacy	November 2000 Complete May 2001	Multicenter, double-blind, placebo-controlled, parallel-group study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 60 mg PO QD Placebo	N = 245 (M = 82; F = 163) 42.4 years (18.6-77.7)	DSM-IV— defined MDD; CGI-Severity score ≥4 at Visits 1 and 2; clinician-rated HAMD ₁₇ total score ≥15 at Visits 1 and 2	9 weeks	HAMD ₁₇ Total Score
F1J-MC- HMBHb; 5.3.5.4.1 (5.3.5.1.2.4); Complete; Full	Safety and Efficacy	November 2000 Complete May 2001	Multicenter, double-blind, placebo-controlled, parallel-group study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 60 mg PO QD Placebo	N = 267 (M = 83; F = 184) 40.9 years (19.2-82.9)	DSM-IV— defined MDD; CGI-Severity score ≥4 at Visits 1 and 2; clinician-rated HAMD ₁₇ total score ≥15 at Visits 1 and 2	9 weeks	HAMD ₁₇ Total Score

Table 5.2.

Study Identifier; Location; Status;		Enrollment Start Status and	Design;	Test and Control Drug(s) Dose, Route,	# Patients (M/F) Mean Age	Diagnosis or Inclusion	Treatment	Primary
Report Type	Objective(s)	End	Control Type	and Regimen	(Range) years	Criteria	Duration	Endpoint
F1J-MC-	Safety and	March 2002	Randomized,	Duloxetine	N = 533	DSM-IV-	38 weeks	Time to
HMBC;	Efficacy	Complete	double-blind,	capsules: 20 mg	(M = 150;	defined MDD;		relapse
5.3.5.4.1		July 2003	placebo-controlled,	Placebo capsules	F = 383	CGI-Severity		during
(5.3.5.1.2.5);			parallel group			score ≥4 at		continuatio
Complete;			study	Duloxetine:	≥18 years	Visits 1 and 2		n phase
Full				60 mg PO QD		and HAMD ₁₇		using the
				Duloxetine		total score		log rank
				60 mg PO BID		≥18 at Visits 1		test
				(Rescue phase)		and 2. Must		
				Placebo		have had one		
						depressive		
						episode.		
F1J-MC-	Safety and	February 2000	Multicenter, long-	Duloxetine	N = 1279	DSM-IV-	52 weeks	Safety
HMAU;	Efficacy	Complete	term, open-label	capsules: 20 mg	(M = 351;	defined MDD;		
5.3.5.4.1		Oct 2001			F = 928)	CGI-Severity		
(5.3.5.2.1);				Duloxetine: 40 –		score ≥3 at		
Complete;				60 mg PO BID	44.4 years	Visits 1 and 2	***************************************	
Full					(18.1-87.4)			

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- HMAG; 5.3.5.4.1 (5.3.5.4.2.1); Complete; Abbreviated	Safety and Efficacy	February 1993 Complete November 1994	Double-blind, stratified, randomized, parallel design with an "enriched" population	Duloxetine tablets: 10 mg Placebo tablets Duloxetine: 20 mg PO QD Placebo	N = 105 (M = 48; F = 57) 40.4 years (19.7-64.7)	DSM-III-R-defined unipolar MDD; for at least 1 month. HAMD ₁₇ total score of ≥17 at Visit I.	10 weeks	HAMD ₁₇ , MADRS Total Scores
F1J-MC- HMAH; 5.3.5.4.1 (5.3.5.4.2.2); Complete; Abbreviated	Safety and Efficacy	November 1993 Complete September 1995	Double-blind, placebo-controlled, randomized, parallel design	Duloxetine tablets: 10 mg Duloxetine tablets: 20 mg Placebo tablets Duloxetine: 20 or 30 mg PO QD Placebo	N = 177 (M = 75; F = 102) 36.5 years (19.1-68.3)	DSM-III-R- defined MDD. HAMD ₁₇ total score of ≥17 at Visit 1.	54 weeks	HAMD ₁₇ , MADRS, CGI-Severity, CGI- Improvement Scores

5.2. tabular-listing

Duloxetine Hydrochloride (LY248686)

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier;		Enrollment		Test and				
Location;		Start		Control Drug(s)	# Patients (M/F)	Diagnosis or		
Status;		Status and	Design;	Dose, Route,	Mean Age	Inclusion	Treatment	Primary
Report Type	Objective(s)	End	Control Type	and Regimen	(Range) years	Criteria	Duration	Endpoint
F1J-MC-	Safety and	December	Randomized,	Duloxetine	N = 648	DSM-III-R-	8-week acute	HAMD ₁₇
HMAI;	Efficacy	1993	parallel, double-	tablets: 5 mg	(M = 212;	defined	phase plus a	Total
5.3.5.4.1		Complete	blind, placebo- and	Duloxetine	F = 436)	unipolar	double-blind	Scores
(5.3.5.4.2.3);		January 1996	active comparator-	tablets: 10 mg		MDD.	extension	
Complete;			controlled study	Duloxetine	42.4 years	HAMD ₁₇ total	phase for a	
Abbreviated				tablets: 20 mg	(17.8-84.1)	score of ≥18.	total of	
				Clomipramine			55 weeks	
				capsules: 25 mg				
				Clomipramine				
				capsules: 50 mg				
				Placebo capsules				
				Duloxetine:				
				5, 10, or 20 mg				
				PO QD				
				Clomipramine:				
				150 mg PO BID				
				Placebo				And the second s

Table 5.2.

Study Identifier; Location;		Enrollment Start		Test and Control Drug(s)	# Patients (M/F)	Diagnosis or		n :
Status;		Status and	Design;	Dose, Route,	Mean Age	Inclusion	Treatment	Primary
Report Type	Objective(s)	End	Control Type	and Regimen	(Range) years	Criteria	Duration	Endpoint
F1J-EW-	Safety and	March 1993	Single arm,	Duloxetine	N = 93	DSM-III-R-	6 weeks	HAMD ₁₇
E001;	Efficacy	Complete	noncontrolled	tablets:	(M = 31; F = 62)	defined		Total
5.3.5.4.1		October 1993		20 mg		unipolar		Scores
(5.3.5.4.2.4);					38.0 years	MDD		
Complete;				Duloxetine:	(18.4-63.8)			***************************************
Abbreviated				20 mg PO QD				

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-US- HMBY; 5.3.5.4.4.7; Ongoing	Safety	June 2002 Ongoing	Double- blind, dose escalation	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60-120 mg PO QD Placebo	Planned: N = 120 total patients Randomized: N = 128 patients Completed acute phase: N = 83 >18 years	DSM-IV- defined MDD; HAMD ₁₇ total score ≥15 at Visits 1 and 2	7 weeks	Safety

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
FIJ-US- HMBZ; 5.3.5.4.4.3; Ongoing; Synopsis	Safety and Efficacy	November 2002 Ongoing	Multicenter, open-label, flexible dose	Duloxetine capsules: 30 mg Duloxetine: 60-120 mg PO QD	Planned: N = 240 total patients Randomized: N = 224 Completed Acute Phase: N = 171 Completed Extension Phase: No patients have completed the extension phase. The study was ongoing as of 01 October 2003 ≥18 years	DSM-IV- defined MDD; HAMD ₁₇ Total score ≥15 and CGI- Severity total score ≥4 at Visits 1 and 2	12 weeks	Compare the stabilized duloxetine dose in treatment-naïve patients and SSRI switch patients

5.2. tabular-listing

Duloxetine Hydrochloride (LY248686)

Table 5.2.

Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- HMBV; 5.3.5.4.4.6; Ongoing; Synopsis	Safety and Efficacy	March 2003 Ongoing	Multicenter, parallel, double-blind, placebo-controlled study of elderly patients (≥65 years of age)	Duloxetine capsules: 30 mg Duloxetine: 60 mg PO QD	Planned = 300 N = 104 (as of 01 October 2003) ≥65 years	At least 65 years of age. Meet criteria for MDD, as defined by DSM- IV. Had a HAMD17 total score ≥ 18 at Visits 1 and 2. Have a MMSE score ≥20 with or without mild dementia.	10 Weeks	Composite cognitive score derived from the VLRT, SDST, 2DCT, and the LNST

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-	Safety and	April 2003	Multicenter,	Duloxetine: 30 mg	Planned: $N = 480$	DSM-IV	12 weeks	Global
HMCQ	Efficacy	Ongoing	randomized,	capsules	Randomized: N =	criteria and		benefit-risk
5.3.5.4.4.4;			double-	Venlafaxine:	285 (as of 01 October	confirmed by		assessment
Ongoing;			blind,	75 mg capsules	2003)	the MINI.		
Synopsis			parallel			HAMD ₁₇		
			study	Duloxetine: 60 to		total score		
		1		120 mg/day PO		≥18 at Visit 1		
				Venlafaxine				
				extended release:				
				150 to 225 mg/day				
				PO				
				Placebo: PO				

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- HMBU 5.3.5.4.4.5; Ongoing Synopsis	Safety and Efficacy	April 2003 Ongoing	Multicenter, randomized, double- blind, parallel study	Duloxetine: 30 mg capsules Venlafaxine: 75 mg capsules Duloxetine: 60 to 120 mg/day PO Venlafaxine extended release: 150 to 225 mg/day PO Placebo: PO	Planned: N = 320 patients. Randomized: N = 89 (as of 25 April 2003)	DSM-IV criteria and confirmed by the MINI. HAMD ₁₇ total score ≥18 at Visit 1	12 weeks	Global benefit-risk assessment

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- HMCN 5.3.5.4.4.2; Ongoing; Synopsis	Safety	Ongoing	Multicenter, open-label study	Duloxetine: 30 mg capsules Duloxetine: 30 mg to 120 mg/day PO	The purpose of this study is to provide treatment with duloxetine to patients who have previously participated in a Lilly sponsored neuroscience clinical trial in countries where it is not currently marketed; therefore there are no limitations to the sample size.	Open-label duloxetine compassionate use study for patients who have previously completed a neuroscience clinical trial	Until duloxetine is commercially available.	Assess the safety of duloxetine, summarize and report spontaneous adverse events

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
FIJ-MC-	Safety and	July 2001	Parallel, double-	Duloxetine	N = 207	Met criteria	12 weeks	FIQ
HMBO	Efficacy	Complete	blind, placebo-	capsules: 20 mg	(M = 23;	for		
Section		March 2002	controlled	Placebo capsules	F = 184)	fibromyalgia		
5.3.5.4.2.1;						as defined by		
Complete;				Duloxetine:	49.1 years	the American		
Full				60 mg PO BID	(18.8-79.7)	College of		
				Placebo		Rheumatology		
						Score of ≥4		
						on the		
						Fibromyalgia		
						Impact		
						Questionnaire		
						at Visits 1		
						and 2.		

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-	Safety and	June 2001	Acute phase:	Duloxetine	Acute phase:	Pain due to	Acute phase:	Weekly
HMAW;	Efficacy	Completed	Double-blind,	capsules: 20 mg	N = 457	bilateral	12 weeks	mean of
Complete;		May 2003	randomized,	Placebo capsules	(M = 281;	peripheral		the 24-
Abbreviated –			parallel, placebo-		F = 176)	neuropathy	Extension	hour
Acute phase;			controlled	Duloxetine:	60.1 years	caused by	phase:	average
5.3.5.1.1.1				60 mg PO BID	(22.4-88.8)	Type I or II	52 weeks	pain
Full –				Duloxetine:		diabetes		severity
Extension				60 mg PO QD	Extension phase:	mellitus.		scores
phase				Duloxetine:	N = 337	Score of at		recorded
5.3.5.2.1				20 mg PO QD	(M = 205;	least 3 on		daily on
				Placebo	F = 132)	MNSI. Daily		an 11-
					59.77 years	pain present		point
					(22.42-88.82)	for \geq 6 month.		Likert
								scale

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- HMBT Section 5.3.5.2.2; Complete 6 month: Abbreviated; Ongoing; extension Clinical synopsis.	Safety and Efficacy	July 2002 Ongoing	Open-label safety study	Duloxetine capsules: 30 mg Duloxetine: 60 mg PO BID Duloxetine: 120 mg PO QD	Planned = 450 6-month Randomized = 449; Completed = 285 ≥18 years	Pain due to bilateral peripheral neuropathy caused by Type I or II diabetes mellitus. Score of at least 3 on MNSI. Daily pain present for ≥6 months.	28 weeks	MNSI
F1J-MC- HMCA; 5.3.5.4.2.2; Ongoing; Synposis	Safety and Efficacy	November 2002 Ongoing	Parallel, double- blind, placebo- controlled study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg BID PO Duloxetine 60 mg QD PO Placebo	Planned = 345 N = 354 (as of 01 October 2003) ≥18 years	Fibromyalgia as defined by the American College of Rheumatology. A score of ≥4 on the average pain item on the BPI at Visit 2.	13 weeks	Brief Pain Inventory- average pain item

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-	Safety and	October 2002	Multicenter,	Duloxetine	Planned = 330	Pain due to	12 weeks	Reduction
HMAVa	Efficacy	Complete	parallel, double-	capsules: 30 mg	Acute N = 334	bilateral diabetic	52-week continuation	in average
		August 2003	blind, randomized,	Placebo capsules	M = 334 M = 204;	neuropathy	Continuation	pain severity as
Acute 5.3.5.1.1.2;			placebo-controlled	Duloxetine:	F = 130	caused by		measured
Complete;				60 mg PO QD	1 = 150)	Type I or II		by an
Full				Duloxetine:	Extension	diabetes		11-point
1 611				60 mg PO BID	N = 223 (as of	mellitus		Likert
Extension				Placebo	01 October			scale
5.3.5.4.2;					2003)			
Synopsis				Routine care				
					≥18 years			
FIJ-MC-	Safety and	October 2002	Multicenter,	Duloxetine	Planned = 330	Pain due to	12 weeks	Reduction
HMAVb;	Efficacy	Ongoing	parallel, double-	capsules: 30 mg	N = 346 (as of	bilateral	52-week	in average
5.3.5.4.2;			blind, randomized,	Placebo capsules	09 December 2003)	diabetic neuropathy	continuation	pain severity as
Ongoing;			placebo-controlled	Duloxetine:	2003)	caused by		measured
Synopsis				60 mg PO QD	≥18 years	Type I or II		by an
				Duloxetine:		diabetes		11-point
				60 mg PO BID		mellitus		Likert
				Placebo				scale
				Routine care				

Duloxetine Hydrochloride (LY248686)

Table 5.2.

Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-US- HMCB 5.3.5.4.4.1; Complete; Abbreviated	Safety and Efficacy	March 2002 Complete November 2002	Double-blind, placebo controlled	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg QD PO Placebo	Planned = 286 N = 178 (M = 98; F = 184) ≥18 years	DSM-IV- defined MDD, HAMD ₁₇ total score ≥15, CGI-Severity total score ≥4 at both Visits 1 and 2, and BPI average	9 weeks	BPI- question 3
						pain score (question 3) of ≥2 at Visit 2		

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
FIJ- MC- SBAT; 5.3.5.4.1 (5.3.5.4.4.1); Complete; Full	Safety and Efficacy	December 2000 Complete April 2002	Double-blind, stratified, randomized, parallel, placebo- controlled, multicenter study Blinded placebo lead-in	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg PO BID Placebo	N = 494 women 52.9 years (24.2-82.6)	SUI Average of at least 7 incontinent episodes per week before enrollment. Positive Cough Stress Test, positive Stress Pad Test result (>2.0 g); first sensation of bladder fill (urge to void) ≥100 mL, bladder capacity >400 mL; normal day and night urinary	12 weeks (subjects completing trial are eligible to continue in Study SBAU)	IEF – percent change from baseline; percent change fo I-QOL total score

5.2. tabular-listing

Duloxetine Hydrochloride (LY248686)

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study	I							1
Identifier;		Enrollment		Test and Control				
Location;		Start		Drug(s)	# Patients (M/F)	Diagnosis or		
Status;		Status and	Design;	Dose, Route, and	Mean Age	Inclusion	Treatment	Primary
•	Objective(s)	End	Control Type	Regimen	(Range) years	Criteria	Duration	Endpoint
Report Type F1J- MC-	Safety and	November	Double-blind,	Duloxetine	N = 683 women	SUI Average	12 weeks	IEF
SBAV;	Efficacy	2000	stratified,	capsules: 20 mg	11 = 005 Women	of at least 7	(subjects	percent
5.3.5.4.1	Efficacy	Complete	randomized,	Placebo capsules	52.8 years	incontinent	completing	change
(5.3.5.4.4.2);		February 2002	parallel, placebo-	Traccoo capsures	(22.5-83.8)	episodes per	trial are	from
		Tebruary 2002	controlled,	Duloxetine:	(22.5 05.0)	week before	eligible to	baseline;
Complete; Full			multicenter study	40 mg PO BID		enrollment.	continue in	percent
ruii			municenter study	Placebo		Positive	Study SBAW)	change for
			Blinded placebo	Taccoo		Cough Stress	Study SB/TVV)	I-QOL
			lead-in			Test, positive		total score
			lead-m			Stress Pad		total score
						Test result		
						(>2.0 g); first		
						sensation of		
						bladder fill		
						(urge to void)		
						≥100 mL,		
						bladder		
						capacity >400		
						mL; normal		
						day and night		
						urinary		
						frequency		

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-	Safety and	May 2001	Double-blind,	Duloxetine	N = 458 women	SUI Average	Duloxetine:	IEF
SBAX;	efficacy	Complete	stratified,	capsules: 20 mg		of at least 7	12 weeks	percent
5.3.5.4.1 (5.3.5.4.4.3);		May 2002	randomized, parallel, placebo-	Placebo capsules	53.2 years (27-79)	incontinent episodes per	Placebo: 12 weeks	change from
Complete;			controlled,	Duloxetine:		week before		baseline;
FuIl			multicenter study	40 mg PO BID		enrollment.		percent
				Placebo		Positive		change for
						Cough Stress		I-QOL total score
						Test, positive Stress Pad		total score
						Test result		
						(>2.0 g); first sensation of		
						bladder fill		
						(urge to void)		
						\geq 100 mL,		
						bladder		
						capacity >400		
				·		mL; normal		
						day and night		
						urinary		
						frequency.		

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SAAW; 5.3.5.4.1 (5.3.5.4.4.4); Complete; Full	Safety and efficacy	June 1998 Complete September 1999	Double-blind, randomized, placebo-controlled study	Duloxetine capsules: 10 mg Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 20, 40, or 80 mg/day PO Placebo	N = 553 women 49.6 years (27.1-65.7)	Subjects with SUI reporting ≥4 incontinent episodes per week	12 weeks	IEF
F1J-MC- SBBL; 5.3.5.4.5.2; Ongoing; Synopsis	Safety and efficacy	June 2001 Ongoing	Double-blind, stratified, randomized, parallel, placebo- controlled, multicenter, pilot study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40-60 mg B1D PO Placebo	Planned = 300 women N = 307 women (as of 15 Dec 2003) 18-78 years	Subjects with bladder overactivity defined as bothersome urinary urgency or UUI for a minimum of three consecutive months	12 weeks	24-hour diary

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
FIJ-MC- SBAF; 5.3.5.4.5.3; Complete	Safety and efficacy	January 2002 Ongoing	Double-blind, randomized, parallel, placebo-controlled multicenter study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg BID PO plus PFMT Placebo plus PFMT	Planned = 200 women N = 201 women (as of 15 Dec 2003) 18-75 years	Subjects with symptoms of SUI, including ≥2 accidental urine leaks per day	Active therapy: 12 weeks Open-label period: until duloxetine is commercially available or the sponsor stops the study	IEF I-QOL
FIJ-MC- SBBA Section 5.3.5.4.5.7; Completed	Safety and efficacy	November 2001 Complete July 2003	Double-blind, randomized, parallel, placebo-controlled. multicenter study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg PO BID Placebo	Planned = 420 women N = 451 women ≥18 years	Subjects with SUI or mixed incontinence for ≥3 months including ≥1 accidental urine leaks per week	36 weeks	I-QOL improvement

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SBAU; 5.3.5.4.5.13; Ongoing; Synopsis	Safety	April 2002 Ongoing	Multicenter, open- label, single- treatment-group extension study to Study FIJ-MC- SBAT	Duloxetine capsules: 20 mg Duloxetine: 40 mg PO BID	N = 363 women (as of 01 October 2003) ≥18 years	Subjects with SUI (who successfully completed SBAT)	Until duloxetine is commercially available for the treatment of UI or sponsor stops the study	Long-term safety data
F1J-MC- SBAW; 5.3.5.4.5.14; Ongoing; Synopsis	Safety	February 2001 Ongoing	Multicenter, open- label, single- treatment-group extension study to Study F1J-MC- SBAV	Duloxetine capsules: 20 mg Duloxetine: 40 mg PO BID	N = 493 women (as of 15 Dec 2003) ≥18 years	Subjects with SUI (who successfully completed SBAV)	Until duloxetine is commercially available for the treatment of UI or the sponsor stops the study	Long-term safety data
F1J-MC- SBAY; 5.3.5.4.5.15; Ongoing; Synopsis	Safety	March 2001 Ongoing	Multicenter, open- label, single- treatment-group	Duloxetine capsules: 20 mg Duloxetine: 40 mg PO BID	Planned = 600 women N = 663 women (as of 15 Dec 2003) ≥18 years	Subjects with SUI for ≥3 months prior to study entry	Until duloxetine is commercially available for the treatment of UI or the sponsor stops the study	Long-term safety data

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SBBM; 5.3.5.4.5.16; Ongoing; Synopsis	Safety	September 2001 Ongoing	Multicenter, open- label, single- treatment-group extension study to Study F1J-MC- SBAX	Duloxetine capsules: 20 mg Duloxetine: 40 mg BID PO	N = 363 women (as of 15 Dec 2003) ≥18 years	Subjects with SUI (who successfully completed SBAX)	Until duloxetine is commercially available for the treatment of SUI or the sponsor stops the study	Long-term safety data
FIJ-MC- SBAB; 5.3.5.4.5.4; Complete	Safety and efficacy	October 2001 Ongoing	Double-blind, randomized, parallel, placebo-controlled, multicenter study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 80 mg/day, given as 40 mg PO BID Placebo	Planned = 50 women N = 65 women (as of 15 Dec 2003) 18-75 years	Subjects with genuine stress incontinence confirmed on urodynamic studies	Active therapy: 4 weeks Open-label extension: duloxetine 40 mg BID until duloxetine is commercially available or the sponsor stops the study	IEF

5.2. tabular-listing

Table 5.2. Tabular Listing of Clinical Studies (continued)

Duloxetine Hydrochloride (LY248686)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SBAM; Acute phase – 5.3,5.4.1	Safety and efficacy	May 2001 Ongoing	Double-blind, stratified, randomized, parallel, placebo- controlled,	Duloxetine capsules: 20 mg Placebo capsules Duloxetine:	Planned = 100 women N = 109 women (as of 15 Dec 2003)	Subjects electing surgery for severe pure genuine stress incontinence	Active period: up to 12 weeks Open-label	Percent change in IEF from baseline to endpoint, and the
(5.3.5.4.4.13); Complete Extension phase – 5.3.5.4.5.11; Ongoing; Synopsis			multicenter study	40-60 mg PO BID Placebo	18-75 years	incontinence	period: until duloxetine is commercially available for the treatment of UI or until the sponsor stops the study	and the change in I-QOL
F1J-MC- SBBX 5.3.5.4.5.12; Ongoing; Synopsis	Safety	December 2002 Ongoing	Open-label, multicountry, multicenter study	Duloxetine capsules: 20 mg Duloxetine: 80-120 mg/day given as 40-60 mg BID	N = 54 women (as of 15 Dec 2003)	Subjects with SUI (who successfully completed SBBL)	52 weeks	PGI-I

5.2. tabular-listing

Duloxetine Hydrochloride (LY248686)

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SAAA; 5.3.5.4.1 (5.3.5.4.5.1); Complete; Full	Safety and efficacy	December 1993 Complete March 1995	Double-blind, randomized, placebo-controlled study	Duloxetine capsules: 20 mg Duloxetine: 20 mg PO QD	N = 92 women	Outpatients diagnosed with either stress, urge, or mixed incontinence	3 weeks	CMG, voiding diary, 24-hour pad test, stress pad test, and social activity questionnaire.
F1J-MC- SAAB; 5.3.5.4.1 (5.3.5.4.5.2); Complete; Abbreviated	Safety and efficacy	August 1995 Complete November 1996	Multicenter, double-blind, placebo-controlled, stratified, randomized, parallel study	Duloxetine capsules: 10 mg, 20 mg Placebo capsules Duloxetine 20, 30, and 40 mg/day PO QD Placebo	N = 288 women 54.8 years (22.2-78.7)	Diagnosis of stress or mixed (with a significant stress component) urinary incontinence	6 weeks	One-hour stress pad test (SPT) weight

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SAAH; 5.3.5.4.1 (5.3.5.4.5.3); Complete; Abbreviated	Safety and efficacy	August 1996 Complete June 1997	Double-blind, placebo-controlled, randomized, parallel study	Duloxetine capsules: 10 mg, 20 mg Placebo capsules Duloxetine: 30, 40 mg/day QD PO Placebo	N = 32 (M = 5; F = 27) 50.5 years (21-75.5)	One of the following diagnoses: urge urinary incontinence, urinary urgency (absent infection) without incontinence, or reflex neurogenic bladder	Double-Blind: Duloxetine: 1 week or Placebo: 1 week Open-Label: Duloxetine: 12 weeks	DAI
F1J-MC- SAAI; 5.3.5.4.1 (5.3.5.4.5.4); Complete; Abbreviated	Safety and efficacy	April 1996 Complete August 1996	Double-blind, placebo-controlled, randomized, parallel study	Duloxetine capsules: 10 mg, 20 mg Placebo capsules Duloxetine: 30, 40 mg/day QD PO Placebo	N = 91men 62.5 years (40.5-85.7)	Diagnosis of mild to moderate BPH	Duloxetine: 8 weeks Placebo: 9 weeks	AUA Symptom Index score

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SAAL; 5.3.5.4.1 (5.3.5.4.5.5); Complete, Abbreviated	Safety and efficacy	May 1996 Complete November 1996	Multicenter, placebo- controlled, double-blind, randomized, crossover study	Duloxetine capsules: 10 mg, 20 mg Oxybutynin capsules: 2.5 mg Placebo capsules Duloxetine: 30/40 mg/day, PO QD Oxybutynin: 7.5/10 mg/day, PO QD Placebo PO QD	N = 68 women 56.88 years (21.87-83.84)	Urinary frequency, urinary urgency, and nocturia	Duloxetine: 4 weeks Oxybutynin: 4 weeks	BUS

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

			_	· · · · · · · · · · · · · · · · · · ·		·		
Study Identifier;		Enrollment Start		Test and Control Drug(s)	# Patients (M/F)	Diagnosis or		
Location;		ł.	D •	1	1	1 -	/m	n .
Status;		Status and	Design;	Dose, Route,	Mean Age	Inclusion	Treatment	Primary
Report Type	Objective(s)	End	Control Type	and Regimen	(Range) years	Criteria	Duration	Endpoint
FIJ-MC-	Safety and	July 2003	Double-blind,	Duloxetine: 40	3600 women	Female	6 weeks	IEF
SBCC;	efficacy	Study ongoing	randomized,	mg BID.	planned	outpatients 18	double blind,	
5.3.5.4.5.1;		Buildy on going	parallel, placebo-	Placebo	437 women	years of age	then open	
Ongoing;			controlled,		randomized (as	with	label until	
Synopsis			multicenter study.		of 15 Dec 2003)	predominant	duloxetine	
					,	SUI	becomes	
						symptoms	commercially	
						will	available for	
						participate in	the treatment	
						this study.	of urinary	
							incontinence	
							in the country	
							where the	
							subject resides	
							or until the	
							sponsor, for	
							any reason	
							stops the	
							study.	

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SBBO 5.3.5.4.5.5; Ongoing; Synopsis	Safety and efficacy	Study ongoing	Study F1J-MC-SBBO is a Phase 3b, double-blind, randomized, parallel, stratified, placebo-controlled, multicenter study of the efficacy of duloxetine compared with placebo in the treatment of women with mixed urinary incontinence (MUI).	Duloxetine: 80 mg/day given as 40 mg capsules twice daily. Placebo	Planned: 600 women Randomized: 292 women have randomized (as of 15 Dec 2003)	Are female outpatients of 18 years of age with symptoms of urinary incontinence based on the disease diagnostic criteria, average a total of at least 4 incontinence episodes per week on the SUIQ, and have had symptoms of urinary incontinence for a minimum of 3 months prior to study entry	8 weeks	IEF

Table 5.2.

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC- SBBT; 5.3.5.4.5.8; Ongoing; Synopsis	Safety and efficacy	July 2003 Study ongoing	Study F1J-MC-SBBT is a double-blind, stratified, randomized, parallel, placebo-controlled, multicenter study of the efficacy of a fixed dose of duloxetine compared with placebo in the treatment of women with SUI.	Duloxetine 80 mg/day given as 40 mg twice daily. Placebo	Planned: 120 women Randomized as of 01 October 2003: 7 women	Are 20 years of age female outpatients with SUI based on the disease diagnostic criteria, average at least one incontinent episode per day on the screening diary, and have had symptoms of SUI for a minimum of 3 months prior to study entry.	12 weeks	IEF

Table 5.2. Tabular Listing of Clinical Studies (continued)

Study Identifier; Location; Status; Report Type	Objective(s)	Enrollment Start Status and End	Design; Control Type	Test and Control Drug(s) Dose, Route, and Regimen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
FIJ-MC- SBBR; 5.3.5.4.5.6; Ongoing; Synopsis	Safety and efficacy	Study ongoing	Double-blind, randomized, parallel, placebo- controlled, multicenter study	Duloxetine 20 mg twice daily (BID) escalating to 40 mg BID Duloxetine 40 mg once daily (QD) escalating to 40 mg BID Duloxetine 40 mg BID Placebo	Planned: 500 women Randomized: 58 women have been randomized (as of 15 Dec 2003)	Are female outpatients 18 years of age and have predominant symptoms of SUI.	12 weeks double-blind, then open label until duloxetine becomes commercially available for the treatment of urinary incontinence in the country where the subject resides or until the sponsor, for any reason, stops the study.	IEF

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Basic Pharmacokinetic and Pharmacodynamic Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center / Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment ^a / Regimen ^b	Duloxetine test product and strength (mg base) ^c	Criteria for Evaluation
F1J-LC- HMAP; 5.3.5.4.1 (5.3.3.1.5); Complete; Abbreviated	Mark J. Goldberg, M.D./ Lilly Laboratory for Clinical Research, Indianapolis, IN / 1 center	Single- blind, randomized placebo- controlled, multiple dose	N = 12 M = 12 (4 received only placebo) F = 0/ Age 22-53	Healthy adult males	21 days/ Placebo x 14.5 days 20 mg BID x 7 days 30 mg BID x 7 days 40 mg BID x 6.5 days	Placebo, 10-mg and 20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyAdverse events, blood pressure, heart rate, ECGs, neurological exams, clinical laboratory tests (serum chemistry, hematology coagulation studies, urinalysis) PharmacokineticPlasma trough concentrations at each dose level and standard multiple-dose pharmacokinetic parameters for duloxetine.
F1J-BD- HMAR 5.3.5.4.1 (5.3.3.1.4); Complete; Full	J.P. Macher, M.D./ Forenap Centre Hospitalier, Rouffach, France/ 1 center	Single- blind, randomized placebo- controlled	N = 14 M = 7 (1 only placebo) F = 7 (1 only placebo)/ Age 23-43	Healthy adults; body mass index (BMI) of 18 to 30	20 days/ Placebo x 2.5 days 20 mg BlD x 2 days 40 mg BID x 6 days 60 mg BID x 6 days 80 mg BID x 5.5 days	Placebo and 20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyPhysical examination, blood pressure, pulse rate, body temperature, weight, ECG, clinical laboratory tests (hematology, urinalysis, and liver tests), adverse events. PharmacokineticStandard multipledose pharmacokinetic parameters for duloxetine at each dose level.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Basic Pharmacokinetic and Pharmacodynamic Studies

Study Identifier;	Study investigator/	Design	Number of subjects	Diagnosis and	Duration of duloxetine	Duloxetine test product	Criteria for Evaluation
Location;	Coordinating		and sex/	criteria	treatmenta/	and strength	2,112
Status;	center /		Age range	for	Regimenb	(mg base) ^c	
Report	Number of		1.26 1	inclusion		(
Туре	center(s)						
FIJ-LC-	Randall Stoltz,	Open-label,	N = 12	Healthy	17 days/	60-mg	SafetyVital signs, ECGs, clinical
HMBN	M.D./	dose	M = 6	adults;	60 mg x 1;	capsules	laboratory tests, clinical assessment and
5.3.5.4.1	West	escalation	F = 6/	Body	60 mg QD x 8	containing	adverse events.
(5.3.3.1.3);	Pharmaceutical		Age 23-61	mass	days;	duloxetine	PharmacokineticStandard single- and
Complete;	Services		-	index	60 mg BID x 7.5	20% w/w	multiple-dose pharmacokinetic
Full	Evansville, IN/			(BMI) <	days	enteric-coated	parameters for duloxetine and
	1 center			35 kg/m ²		pellets	metabolites.
F1J-LC-	D.L. Hyslop,	Single-	N = 9	Healthy	5 weeks	5 mg – 80 mg	Safety—Clinical laboratory tests,
HMAB	M.D./	blind,	M = 9	adults;		capsules	nervous system examination, pupil size,
5.3.5.4.1	Lilly Laboratory	placebo-	Ages 26-55	Body		containing	blood pressure measurements, ECGs.
(5.3.3.1.9);	for Clinical	controlled		mass		duloxetine	PharmacokineticStandard single- and
Complete;	Research			index		20% w/w	multiple-dose pharmacokinetic
Full	Indianapolis, IN/			(BMI) <		enteric-coated	parameters for duloxetine and
	1 center			35 kg/m ²		pellets	metabolites.
F1J-LC-	Michael H.	Open-label,	N = 4	Healthy	20.2 mg single	20.2 mg ¹⁴ C-	SafetyVital signs, ECGs, routine
SAAZ	Skinner, M.D./	single-dose	M = 3	adults	dose	labeled	laboratory tests, clinical assessment, and
5.3.5.4.1	Lilly Laboratory		F = 1/	within		(100 μCi)	adverse events.
(5.3.3.1.1);	for Clinical		Age 37-48	30% of		duloxetine	PharmacokineticStandard single-dose
Complete;	Research			ideal body		enteric-coated	pharmacokinetic parameters for
Full	Indianapolis, IN/			weight		tablet	duloxetine and total radioactivity.
	1 center						Metabolite identification
							Elimination pathways

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Basic Pharmacokinetic and Pharmacodynamic Studies

Study	Study	Design	Number of	Diagnosis	Duration of	Duloxetine	Criteria for
Identifier;	investigator/		subjects	and	duloxetine	test product	Evaluation
Location;	Coordinating		and sex/	criteria	treatment ^a /	and strength	
Status;	center /		Age range	for	Regimen ^b	(mg base)c	
Report	Number of			inclusion			
Туре	center(s)						
F1J-LC-	Michael H.	Open-label,	N = 14	Healthy	4 days/	20-mg	SafetyVital signs, ECGs, routine
SBAA;	Skinner, M.D./	4-way	$\mathbf{M} = 0$	adult	40mg x 4 with 1	capsules	laboratory tests, and adverse events.
5.3.5.4.1	Lilly	crossover,	F = 14 /	females;	week washout	containing	PharmacokineticStandard single-
(5.3.3.4.4);	Laboratory for	(fasting x 2;	Age 18-50	within	between each dose	duloxetine	dose pharmacokinetic parameters for
Complete;	Clinical	high fat		30% of		10% w/w	duloxetine.
Full	Research/	breakfast		ideal body		enteric-coated	
	Indianapolis,	and		weight		pellets	
	IN/1 center	bedtime)					
F1J-LC-BD-	Michel	Randomized	N = 12	Healthy	7 days/	20-mg	Safety Electrocardiogram,
0001;	Guillaume,	, double-	M = 12	adult	80 mg QD x 7 days	capsules	laboratory tests, recording of
5.3.5.4.1	M.D./	blind,	F = 0/	males;	(n=6) 60 mg BID x	containing	symptoms and vital signs.
(5.3.4.1.2.);	Aster-Cephac	3-period	Age 23-38	extensive	6.5 days (n=6);	duloxetine	PharmacokineticPlasma
Complete	Paris, France/	cross-over,		metaboliz	Desipramine 50 mg	10% w/w	concentration measurements of
	1 center	placebo- and		ers with	BID x 6.5 days	enteric-coated	duloxetine and desipramine (No
		desipramine		regard to	Placebo x 6.5 days	pellets	formal PK analyses performed)
		-controlled,		CYP2D6			PharmacodynamicPressor response
		evaluating 2		phenotype			to IV bolus injection of tyramine; 24
		regimens of					hour urinary catecholamines and
		duloxetine					metabolites; Whole blood 5-HT;
							Polygraphic sleep recordings
							(hypnographic EEG parameters);
							Leeds sleep questionnaires.

Table 5.2. Tabular Listing of Clinical Studies (concluded)

Clinical Pharmacology-Basic Pharmacokinetic and Pharmacodynamic Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center / Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-LC-BD- SBBN; 5.3.5.4.1 (5.3.4.1.1); Complete; Full	David Robertson, M.D./ Vanderbilt University Medical Center, Nashville, TN/ I center	Single-blind, randomized, outpatient study	N= 15 M= 5 F= 10 Age 18-39	Overtly healthy male and female subjects	14 days/ 40 mg/BID x 14 days, increasing by 40 mg each week up to 240 mg daily doses (120 mg/BID).	20 mg Capsule free base containing 20% w/w enteric-coated pellets	Safety— Safety parameters included vital signs, electrocardiograms, clinical laboratory values, and adverse events. Pharmacokinetic—No formal pharmacokinetic analysis was performed for duloxetine. Three concentration measurements of duloxetine were summarized descriptively and evaluated graphically. Pharmacodynamic— Pharmacodynamic analyses will be presented in the completed study report.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Bioavailability/ Bioequivalence Studies

Study Identifier; investigato Location; Coordinati Status; center / Report Number of Cype center(s)	I	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-LC- HMBG 5.3.5.4.1 (5.3.1.2.1); Complete; Full Research Indianapoli IN/ 1 center	single-dose, two period, crossover	N=26 M=6 F=20/ Age 22-65	Healthy males or females; Body mass index (BMI) less than 35 kg/m ²	2 days/ 60 mg x 2 separated by 7 -21 day washout	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets (clinical trial formulation) and 60-mg capsules containing duloxetine 20% w/w enteric-coated	SafetyVital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. PharmacokineticStandard single-dose pharmacokinetic parameters for duloxetine_Standard bioequivalence criteria based on C _{max} and AUC.

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Bioavailability/ Bioequivalence Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center / Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-LC- HMBI; 5.3.5.4.1 (5.3.1.1.1); Complete; Full	Michael A. Turik, M.D./ Lilly Laboratory for Clinical Research/ Indianapolis, IN/ 1 center	This is a two part, open-label study with a randomized, two-period, crossover design in Part B of the study.	N= 10 M= 5 F= 5 Age 21-58	Overtly healthy male and female subjects.	IV duloxetine: Part A: 0.8 mg duloxetine single dose given intravenously over a 30-minute period; Part B: 10-mg duloxetine single dose given intravenously over a 30-minute period. Oral duloxetine: Parts A and B: 60-mg duloxetine single dose given orally as 60-mg capsule one week after the IV dose	IV duloxetine HCl equivalent to 0.8 mg duloxetine (Part A) or 10 mg duloxetine (Part B) Duloxetine HCl as encapsulated enteric-coated pellets (20%) equivalent to 60-mg duloxetine.	Safety Safety parameters included vital signs, clinical laboratory tests, and adverse events. Pharmacokinetic Single-dose pharmacokinetic parameters including maximal plasma concentration (C_{max}), time to C_{max} (T_{max}), area under the curve (AUC), plasma clearance (CL or CL/F), volume of distribution ($V_{\lambda Z}$ or $V_{\lambda Z}$ /F), elimination rate constant (λ_Z), elimination half-life ($t_{1/2}$), mean absorption time (MAT), mean residence time (MRT), and absolute bioavailability (F).

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Pharmacokinetics Studies (Special Populations)

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center / Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment ^a / Regimen ^b	Duloxetine test product and strength (mg base) ^c	Criteria for Evaluation
F1J-LC- HMAX; 5.3.5.4.1 (5.3.3.3.3); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN USA and Robert A. Branch M.D/ Univ. of Pittsburgh Medical Center, Pittsburgh, PA/ 2 centers	Open- label, single dose	N = 13 M = 11 (5 cirrhotic, 6 healthy) F = 2 (1 cirrhotic, 1 healthy)/ Age 20-63	Adults with moderate cirrhosis (Child-Pugh Class B); Controls: age and sex matched healthy adults	I day/ 20 mg single dose	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyVital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. PharmacokineticStandard single-dose pharmacokinetic parameters for duloxetine and metabolites.
F1J-LC- HMBJ; 5.3.5.4.1 (5.3.3.3.2); Complete; Full	William B. Smith, M.D./ New Orleans Center for Clinical Research and Randall R. Stoltz, M.D./ West Pharmaceutical Services Evansville, IN/ 2 centers	Open- label, single dose	N = 24 M = 20 F = 4 Age 19-61	Adults with end stage renal disease on hemodialysis Controls: age and sex matched healthy adults	1 day/ 60 mg single dose	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyECGs, orthostatic blood pressure and pulse rate measurements, body weight, vital signs, clinical laboratory testing PharmacokineticStandard single-dose pharmacokinetic parameters for duloxetine and metabolites.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology-Pharmacokinetics Studies (Special Populations)

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center / Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment ^a / Regimen ^b	Duloxetine test product and strength (mg base) ^c	Criteria for Evaluation
F1J-LC- SAAY; 5.3.5.4.1 (5.3.3.3.1); Complete; Full	H. Wayne Hutman, M.D./ South Florida Bioavailabilit y Clinic Miami, FL/ 1 center	Open-label, single-dose	N = 24 M = 0 F = 24 Age 32-50 n = 12 Age 65-77 n = 12	Healthy female subjects within 30% of ideal body weight	1 day/ 40 mg single dose	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyVital signs (systolic and diastolic blood pressure, heart rate), ECG, clinical laboratory tests (clinical chemistry, hematology), and adverse events. PharmacokineticStandard single-dose pharmacokinetic parameters for duloxetine.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology Drug Interaction Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center/ Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Reginien	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-LC- HMAZ; 5.3.5.4.1 (5.3.3.4.1); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN / I center	Open-label multiple dose sequential crossover	N = 16 M= 7 F = 9 / Age 21-63	Healthy subjects with body mass index less than 30 kg/m ²	21 days/ duloxetine 40 mg BID x 6 days 60 mg BID x 15 days desipramine 50 mg alone and then with 60 mg BID duloxetine	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetySafety parameters included vital signs, ECGs, clinical laboratory tests, and adverse events PharmacokineticStandard multipledose pharmacokinetic parameters for duloxetine and standard single-dose pharmacokinetic parameters for desipramine.
F1J-LC- HMBA; 5.3.5.4.1; (5.3.3.4.10)	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN/ I center	Randomized Single blind, three-period cross over (at least 1 week washout between periods)	N = 16 M = 6 F = 10 / Age 21-58	Healthy adults with body mass index (BMI) less than 30 kg/m ²	2 days/ duloxetine 60 mg alone, ethanol 10% alone, and duloxetine 60 mg with ethanol 10%	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetySafety parameters included vital signs, ECGs, clinical laboratory tests, and adverse events. PharmacokineticPlasma duloxetine concentrations and blood ethanol concentrations of ethanol. (No formal PK analyses were performed) PharmacodynamicMeasures included Alcohol Effects Scale questionnaire and Automated Performance Test System

Duloxetine Hydrochloride (LY248686)

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology Drug Interaction Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center/ Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-FW- HMBB; 5.3.5.4.1 (5.3.3.4.5); Complete; Full	Stephen D. Wise, B.Med. Sci. MB. ChB. FRCP. FFPM/ Lilly-NUS Centre for Clinical Pharmacology Pte. Ltd., Singapore/ 1 center	Open-label, randomized, 4-period crossover study (at least 4-day washout each period)	N = 14 M = 14 F = 0 / Age 21-38	Healthy adults with body mass index (BMI) 19- 30 kg/m ²	4 days/ 4 single 60 mg doses duloxetine 60 mg alone, with antacid, with famotidine, and with activated charcoal	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyPhysical examination, vital signs, ECGs, clinical laboratory evaluations. PharmacokineticStandard single-dose pharmacokinetic parameters for duloxetine.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology Drug Interaction Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center/ Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-BD- HMBD; 5.3.5.4.1 (5.3.3.4.11); Complete; Full	J. P. Macher, M.D./ Forenap Centre Hospitalier, Rouffach, France/ 1 center	Randomized double-blind, two-period, cross-over study (at least 10-day washout after each period)	N = 16 M = 8 F = 8/ Age 21-45	Healthy adults	8 days/ Duloxetine 60 mg BID x 7.5 days; Placebo BID x 7.5 days; Lorazepam 2 mg BID given concurrently for last 3.5 days	Placebo and 20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	SafetyVital signs, ECGs, clinical laboratory tests, adverse events. Pharmacokinetic—Standard multiple-dose pharmacokinetic parameters for duloxetine and lorazepam. PharmacodynamicImmediate and delayed word recall assessing cognitive effects; Critical flicker fusion threshold test assessing cortical alertness/information processing; Multiple choice reaction time assessing psychomotor performance; Digit symbol substitution test assessing psychomotor performance; Bond & Lader visual analog scale and subjective evaluation of vigilance and mood.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology Drug Interaction Studies

Study Identifier; Location; Status; Report Type	scology Drug Inte Study investigator/ Coordinating center/ Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-BD- HMBF; 5.3.5.4.1 (5.3.3.4.3); Complete; Full	Jean-Philippe Decourt, M.D./ Parexel Clinical Pharmacology Poitiers, France/ I center	Randomized single-blind, two-way balanced cross-over study (at least 10-day washout after each period)	N = 11 M = 11 F = 0/ Age 23 - 46	Healthy non- smoker male adults with body mass index 18 to 28	5 days/ Duloxetine 60 mg BID x 4.5 days; Placebo BID x 4.5 days; Aminophylline 250 mg intravenous solution (197.5 mg theophylline)	Placebo and 20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	Safety Safety parameters included vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinetic—Standard singledose pharmacokinetic parameters for theophylline and urinary excretion of theophylline and the metabolites.
F1J-FW- SBAG; 5.3.5.4.1 (5.3.3.4.2); Complete; Full	Dr. Stephen D. Wise, B.Med. Sci. MB. ChB. FRCP. FFPM / Lilly-NUS Centre for Clinical Pharmacology Pte. Ltd., Singapore/ 1 center	Open-label, sequential two-period study (separated by 4-day washout period)	N = 12 M = 12 F = 0 / Age 21-27	Healthy adults with body mass index (BMI) 19- 30 kg/m ²	10 days/ Duloxetine 40 mg QD x 4.5 days; Paroxetine 20 mg QD x 20 days with concomitant duloxetine from days 12 through 16.	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	Safetyphysical examination, vital signs, ECGs, clinical laboratory evaluations Pharmacokinetic—Standard multipledose pharmacokinetic parameters for duloxetine.

Table 5.2. Tabular Listing of Clinical Studies (continued)

Clinical Pharmacology Drug Interaction Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center/ Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-FW-	Dr. Stephen D.	Double-	N= 16	Healthy	5 days, 80 mg/day,	20 mg	Safety - Physical examination, vital
SBAS;	Wise, B.Med.	blinded,		CYP2D6	given as two	Capsules	signs, 12-lead electrocardiogram
5.3.5.4.1	Sci. MB. ChB.	randomized	M=3	extensive	divided 40-mg	containing	(ECG) and adverse events.
(5.3.3.4.9);	FRCP. FFPM/	, 2 period	F= 13	metaboliz	doses (2x20 mg	duloxetine	Pharmacokinetics – Steady-state
Complete;	Lilly-NUS	crossover		er males	capsules)	20% w/w	pharmacokinetic parameters for
Full	Centre for	study.	Age 21-65	or females		enteric-coated	tolterodine and its 5-hydroxymethyl
	Clinical				5 days /Duloxetine	pellets	metabolite (5-HM) including maximal
	Pharmacology				Placebo: for one		plasma concentration ($C_{max,ss}$), time
	Pte. Ltd.,				period		to $C_{max,ss}$ ($T_{max,ss}$), area under the
	Singapore/						curve (AUC _{τ,ss}), elimination rate
	1 center				5 days /Tolterodine:		constant (λ_z) and half-life $(t_{1/2})$.
					for each of the two		Apparent plasma clearance and
					periods		volume of distribution were only
							evaluated for tolterodine.
							Predose and 12-hour concentration
							values of duloxetine were used to
							assess steady-state attainment.

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Clinical and Pharmacokinetic Study Summary

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
FIJ-LC- HMAO; 5.3.5.4.1 (5.3.1.2.2); Complete; Abbreviated	Mark J. Goldberg, M.D. Lilly Laboratory for Clinical Research One	Seven different single- dose treatment regimens	N = 14 M = 14	Healthy male subjects	1 day; Duloxetine 20-mg enteric-coated tablet po in the morning (fasting). Duloxetine 20-mg enteric-coated tablet po at bedtime (fasting). Duloxetine 20-mg capsule containing enteric-coated pellets po in the morning (fasting). Duloxetine 20-mg capsule containing enteric-coated pellets po in the morning (fasting). Duloxetine four 5-mg capsules containing enteric-coated pellets po in the morning (fasting). Duloxetine 20-mg capsules containing enteric-coated pellets po in the morning enteric-coated pellets po in the morning before a standardized breakfast (fed). Duloxetine four 5-mg capsules containing enteric-coated pellets po in the morning before a standardized breakfast (fed).	Duloxetine 5 mg 20 mg	Safety and Tolerability

 Table 5.2.
 Tabular Listing of Clinical Studies (continued)

Healthy Subject PK and Initial Tolerability Studies

Study Identifier; Location;	Study investigator/ Coordinating center Number of center(s)	Design	Number of subjects and sex/	Diagnosis and criteria for	Duration of duloxetine treatment/	Duloxetine test product and strength (mg base)	Criteria for Evaluation
Status; Report Type			Age range	inclusion	Regimen		
FIJ-LC- HMAF 5.3.5.4.1 (5.3.3.1.2); Complete; Full	N/A Lilly Laboratory for Clinical Research	N/A	N/A	Healthy Subjects	N/A	N/A	Safety and Tolerability
F1J-LC- SBCH(a) 5.3.3.1.1; Complete; Synopsis	Michael Turik, MD Lilly Laboratory for Clinical Research One	Open-label Dose- Escalation Study	N = 12 F = 12 18-75 years	Healthy Female Subjects	14 Days 60 mg BlD x 1-3 days 120 mg BID x 1-3 days 160 mg BID x 4 days 200 mg BID x 3½ days	Duloxetine 20 mg 30 mg	Safety and Tolerability

Table 5.2. Tabular Listing of Clinical Studies (continued)

Healthy Subject PK and Initial Tolerability Studies

Study	Study investigator/	Design	Number of	Diagnosis	Duration of	Duloxetine test	Criteria for
Identifier;	Coordinating center		subjects	and criteria	duloxetine	product and	Evaluation
Location;	Number of center(s)		and sex/	for	treatmenta/	strength (mg base)c	
Status;			Age range	inclusion	Regimenb		
Report Type							
F1J-LC-	Dr. K. Rathgen	Randomi	Planned:	Healthy	7 days	Duloxetine to 20 mg	Safety:
SBCG;	Human Pharmacology Centre	zed,	32 subjects	female	Duloxetine 20	capsules, 5 capsules	Tolerability
5.3.3.1.2;	Boehringer Ingelheim Pharma	placebo	(12* 40	subjects as	mg capsules	twice daily or	(adverse events),
Complete;	GmbH & Co. KG	controlle	mg; 12*	determined	40 mg or 100	Duloxetine 20 mg 2	ECG, systolic and
Synopsis	D-88397 Biberach / Riss	d, double	100 mg; 8*	by results of	mg BID	capsules twice daily	diastolic blood
	Clinical Research	blind	placebo)	screening.	po	and 3 capsules	pressure, routine
	1 Center	trial.		Signed		placebo twice daily	labs.
			Randomize	written		given orally.	
			d: 32	informed			
			subjects	consent in			
				accordance			
			Completed:	with GCP		The second secon	
Name of the last o			26 subjects	and local			
***				legislation.			
				Age ≥ 40			
				years . BMI			
				≥ 18.5 and ≤			
				29.9 kg/m ²			
F1J-LC-	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HMAD;							
5.3.5.4.1							
(5.3.3.1.6);							
Complete							

5.2. tabular-listing

Duloxetine Hydrochloride (LY248686)

Table 5.2. Tabular Listing of Clinical Studies (continued)

Healthy Subject PK and Initial Tolerability Studies

Study Identifier; Location; Status; Report Type	Study investigator/ Coordinating center Number of center(s)	Design	Number of subjects and sex/ Age range	Diagnosis and criteria for inclusion	Duration of duloxetine treatment/ Regimen	Duloxetine test product and strength (mg base)	Criteria for Evaluation
F1J-LC- HMAA; 5.3.5.4.1 (5.3.3.1.7); Complete; Synopsis	U.S. Schwertschlag Lilly Laboratory for Clinical Research One	Single-blind, placebo- controlled	N = 3 M = 3 21-55 years	Healthy adult males	Single dose	Duloxetine 5-mg capsules 10-mg capsules 25-mg capsules Placebo	Safety and Pharmacokinetics
F1J-FW- SBAZ; 5.3.5.4.1 (5.3.3.1.11); Complete; Full	Alan G Moskwa, MD CMAX, a Division of Institute of Drug Technology Australia Limited One	A double-blinded, randomized, three-period crossover study involving 2 ethnic groups of Japanese and Caucasians	Part A Japanese subjects: Male 10, Female 15, Caucasian subjects: Male 12, Female 14, Part B Japanese subjects: Male 14, Female 6, Caucasian subjects: Male 15, Female 6 20-50 Years	Healthy -Japanese -Caucasian	Part A: Duloxetine HCl: 20 mg, 40 mg and 60 mg were given as 3 single doses to each subject Part B: Duloxetine HCl: 20 mg BID or 40 mg BID	Duloxetine 20 mg	Safety and Pharmacokinetics

Table 5.2. Tabular Listing of Clinical Studies (continued)

Extrinsic Factor PK Study Reports

Study	Study investigator/	Design	Number of	Diagnosis	Duration of	Duloxetine	Criteria for
Identifier;	Coordinating center /		subjects and sex/	and	duloxetine	test product	Evaluation
Location;	Number of center(s)		Age range	criteria	treatment/	and	
Status;				for	Regimen	strength	
Report Type				inclusion		(mg base)	
F1J-LC-	Michael H. Skinner, M.D.,	Randomized,	14	4 Weeks	Duloxetine 60	Duloxetine	Drug-Drug
HMCC;	Pharm.D.	open label 4-			mg orally,	capsules, 20	Interaction
5.3.5.4.1	Lilly Laboratory for	arm sequential	Males	Male	single dose	mg	Study
(5.3.3.4.8);		treatment		Smokers	1	Duloxetine	
Complete;	Clinical Research	crossover study			(two	IV, 10 mg	
Full			18-65 Years		occasions)		
		Section 1					
					Duloxetine:		
	One				10 mg		
					intravenous		
					solution, single		
					dose (two		
					occasions)		-

Table 5.2. Tabular Listing of Clinical Studies (continued)

Reports of Human Pharmacodynamics (PD) Studies

Study	Study investigator/	Design	Number of	Diagnosis	Duration of	Duloxetine test	Criteria for
Identifier;	Coordinating center /		subjects and	and criteria	duloxetine	product and	Evaluation
Location;	Number of center(s)		sex/	for inclusion	treatment/	strength (mg	
Status;			Age range		Regimen	base)	
Report Type							
FIJ-LC-	D. L. Hyslop, MD	Double-blinded,	N = 12	Healthy male	68 days	Duloxetine (low	Safety
HMAE;	U. S. Schwertschlag,	randomized,	M = 12	subjects	(duloxetine 5	dose): 5.0 mg/day,	
5.3.5.4.1	MD, PhD	three-way			mg QD for 14		
(5.3.4.1.3);		crossover study			days;	Duloxetine (high	
Complete;	Lilly Laboratory for				duloxetine 20	dose): 20.0	
Full	Clinical Research				mg QD for 14	mg/day,	
					days; placebo		
	One				for 40 days)	Placebo,	
F1J-MC-	N/A	N/A	N/A	N/A	N/A	N/A	N/A
SAAN;						,	
5.3.5.4.1							
(5.3.4.1.4);							
Complete;							
Abbreviated							

Table 5.2. Tabular Listing of Clinical Studies (continued)

Reports of Human Pharmacodynamics (PD) Studies

Study	Study investigator/	Design	Number of	Diagnosis	Duration of duloxetine	Duloxetine test	Criteria for
Identifier;	Coordinating center /		subjects	and criteria	treatment/	product and	Evaluation
Location;	Number of center(s)		and sex/	for inclusion	Regimen	strength (mg	
Status;			Age range			base)	
Report Type							
FIJ-LC-	James C. Kisicki, MD	single-blinded,	N = 12	Healthy male	18 days	Duloxetine	Drug-Drug
HMAJ;		sequential	M = 12	subjects	Treatment 1: One	20 mg	Interaction
5.3.5.4.1	Harris Laboratories, Inc.	dosing			capsule of Restoril _ 30		Study
(5.3.3.4.7)			19-55 years		mg and one tablet	Restoril	
Complete;	One				duloxetine placebo as a	30 mg	
Clinical					combination dose with		
Study					240 mL water at 11:00	Placebo	
Summary					PM.		
					Treatment 2: One tablet		
					duloxetine 20 mg and		
					one capsule temazepam		
					placebo as a		
					combination dose with		
					240 mL water at 11:00		
					PM.		
					Treatment 3: One tablet		
					duloxetine 20 mg and		
					one capsule Restoril _		
					30 mg as a		
					combination dose with		
					240 mL water at 11:00		
					PM.		

Table 5.2. Tabular Listing of Clinical Studies (continued)

Studies Conducted By Shionogi & Co.

Study	Location
F1J-JE-102G	5.3.5.4.1
	(5.3.5.4.6.4)
F1J-JE-221G	5.3.5.4.1
F1J-JE-301G	(5.3.5.4.6.5)
L11-1E-201Q	(5.3.5.4.6.2)
F1J-JE-311G	5.3.5.4.1
	(5.3.5.4.6.6)
F1J-JE-312G	5.3.5.4.1
	(5.3.5.4.6.7)
F1J-JE-313G	5.3.5.4.1
	(5.3.5.4.6.8)
F1J-JE-321G	5.3.5.4.1
(acute phase)	(5.3.5.4.6.9)
F1J-JE-321G	5.3.5.4.1
(compassionate	(5.3.5.4.6.1)
use phase)	
F1J-JE-322G	5.3.5.4.1
	(5.3.5.4.6.11)

Table 5.2. Tabular Listing of Clinical Studies (concluded)

Studies Conducted By Shionogi & Co.

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Study	Location
F1J-JE-323G	5.3.5.4.1
	(5.3.5.4.6.12)
F1J-JE-324G	5.3.5.4.1
	(5.3.5.4.6.13)
F1J-JE-401G	5.3.5.4.1
(Urge Study)	(5.3.5.4.6.3)
F1J-JE-1008	5.3.5.4.1
	(5.3.5.4.6.14)
F1J-JE-1009	5.3.5.4.1
	(5.3.5.4.6.15)

Abbreviations: 2DCT = 2-Digit Cancellation Test; 5-HT = serotonin; AUA = American Urological Association Symptom Index; AUC = area under the curve; BMI = body mass index; BUS = Behavioral Urge Score; BID = twice daily; BPI = Brief Pain Inventory; CGI-Improvement = Clinical Global Impressions of Improvement; CGI-Severity = Clinical Global Impressions of Severity; CL = plasma clearance; CL/F = Cmax = apparent plasma clearance; maximum plasma concentration; CMG = cystometrogram; DAI = detrusor activity index; DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; ECG = electrocardiogram; F = female; HAMD17 = 17-item Hamilton Depression Rating Scale; IEF = incontinence episode frequency; 1-QOL = Incontinence Quality of Life Questionnaire; IV = intravenous; LNST = Letter-Number Sequencing Test; M = male; MAT = mean absorption time; MDD = major depressive disorder; MINI = Mini International Neuropsychiatric; Interview; MNSI = Michigan Neuropathy Screening Instrument; MRT = mean residence; N = number of subjects; PGI-Improvent = Patient's Global Impressions of Improvement; PK = pharmacokinetic; PO = orally; QD = once daily; SDST = Symbol Digit Substitution Test; SPT = stress pad test; SSRI = selective serotonin reuptake inhibitor; SUI = stress urinary incontinence; Tmax = time to maximum concentration; UI = urinary incontinence; UUI = urge urinary incontinence; VLRT = Verbal Learning and Recall Test.