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; 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-HMAQ(a); 5.3.5.4.1 (5.3.5.1.2.1); Complete; Full	Safety and Efficacy	February 1999 Complete May 2000	Multicenter, parallel group, double-blind, randomized placebo-controlled, blinded placebo lead-in and lead-out	Duloxetine capsules: 10 mg, 20 mg Fluoxetine capsules: 20 mg Placebo capsules Duloxetine: 20-60 mg PO BID Fluoxetine: 20 mg PO QD Placebo	N = 173 (M = 62; F = 111) 41.4 years (18.7-65)	DSM-IV-defined MDD (current episode duration ≥2 weeks); CGI-Severity Score ≥4; clinician-rated $HAMD_{17}$ total score ≥15 at Visits 1 and 2	8 weeks	$HAMD_{17}$ Total Score

(continued)

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-HMAQ(b); 5.3.5.4.1 (5.3.5.1.2.2); Complete; Full	Safety and Efficacy	March 1999 Complete January 2001	Multicenter, parallel group, double-blind, randomized placebo-controlled, blinded placebo lead-in and lead-out	Duloxetine capsules: 10 mg, 20 mg Fluoxetine capsules: 20 mg Placebo capsules Duloxetine: 20-60 mg PO BID Fluoxetine: 20 mg PO QD Placebo	N = 194 (M = 65; F = 129) 40.4 years (18.9-64.4)	DSM-IV–defined MDD (current episode duration ≥2 weeks); CGI-Severity score ≥4; clinician-rated $HAMD_{17}$ total score ≥15 at Visits 1 and 2	8 weeks	$HAMD_{17}$ Total Score

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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-HMATb; 5.3.5.4.1 (5.3.5.1.1.1); Complete; Full	Safety and Efficacy	March 2000 Complete February 2001	Multicenter, parallel, double-blind, randomized, placebo- and active comparator-controlled study with blinded placebo lead-in and placebo lead-out	Duloxetine capsules: 20 mg Paroxetine capsules: 20 mg Placebo capsules Duloxetine: 20 mg or 40 mg PO BID Paroxetine: 20 mg PO QD Placebo	N = 353 (M = 136; F =217) 40.5 years (18.2-78.2)	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	8 weeks	$HAMD_{17}$ Total Score
F1J-MC-HMATa; 5.3.5.4.1 (5.3.5.1.1.2); Complete; Full	Safety and Efficacy	March 2000 Complete April 2001	Multicenter, parallel, double-blind, randomized, placebo- and active comparator-controlled study with blinded placebo lead-in and placebo lead-out	Duloxetine capsules: 20 mg Paroxetine capsules: 20 mg Placebo capsules Duloxetine: 20 mg or 40 mg PO BID Paroxetine: 20 mg PO QD Placebo	N = 354 (M = 136; F = 218) 43.7 years (18.0-82.2)	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	8 weeks	$HAMD_{17}$ Total Score

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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-HMAYa 5.3.5.4.1; (5.3.5.1.1.3); Complete; Full	Safety and Efficacy	November 2000 Complete July 2002	Multicenter, parallel, double-blind, randomized, placebo- and active comparator-controlled study with blinded placebo lead-in and placebo lead out	Duloxetine capsules: 20 mg Paroxetine capsules: 20 mg Placebo capsules Duloxetine: 40 or 60 mg PO BID Paroxetine: 20 mg PO QD Placebo	N = 367 (M = 100; F =267) 43.4 years (19.3-74.4)	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	34 weeks	$HAMD_{17}$ Total Score
F1J-MC-HMAYb 5.3.5.4.1; (5.3.5.1.1.4); Complete; Full	Safety and Efficacy	October 2000 Complete July 2002	Multicenter, parallel, double-blind, randomized, placebo- and active comparator-controlled study with blinded placebo lead-in and placebo lead out	Duloxetine capsules: 20 mg Paroxetine capsules: 20 mg Placebo capsules Duloxetine: 40 or 60 mg PO BID Paroxetine: 20 mg PO QD Placebo	N = 392 (M = 119; F = 273) 45.2 years (20.1-76.7)	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	34 weeks	$HAMD_{17}$ Total Score

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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

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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-HMBC; 5.3.5.4.1 (5.3.5.1.2.5); Complete; Full	Safety and Efficacy	March 2002 Complete July 2003	Randomized, double-blind, placebo-controlled, parallel group study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 60 mg PO QD Duloxetine 60 mg PO BID (Rescue phase) Placebo	N = 533 (M = 150; F = 383) ≥18 years	DSM-IV–defined MDD; CGI-Severity score ≥4 at Visits 1 and 2 and $HAMD_{17}$ total score ≥18 at Visits 1 and 2. Must have had one depressive episode.	38 weeks	Time to relapse during continuation phase using the log rank test
F1J-MC-HMAU; 5.3.5.4.1 (5.3.5.2.1); Complete; Full	Safety and Efficacy	February 2000 Complete Oct 2001	Multicenter, long-term, open-label	Duloxetine capsules: 20 mg Duloxetine: 40 – 60 mg PO BID	N = 1279 (M = 351; F = 928) 44.4 years (18.1-87.4)	DSM-IV–defined MDD; CGI-Severity score ≥3 at Visits 1 and 2	52 weeks	Safety

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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 $\geq$17 at Visit 1.	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 $\geq$17 at Visit 1.	54 weeks	$HAMD_{17}$, MADRS, CGI-Severity, CGI-Improvement Scores

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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-HMAI; 5.3.5.4.1 (5.3.5.4.2.3); Complete; Abbreviated	Safety and Efficacy	December 1993 Complete January 1996	Randomized, parallel, double-blind, placebo- and active comparator-controlled study	Duloxetine tablets: 5 mg Duloxetine tablets: 10 mg Duloxetine tablets: 20 mg Clomipramine capsules: 25 mg Clomipramine capsules: 50 mg Placebo capsules Duloxetine: 5, 10, or 20 mg PO QD Clomipramine: 150 mg PO BID Placebo	N = 648 (M = 212; F = 436) 42.4 years (17.8-84.1)	DSM-III-R-defined unipolar MDD. $HAMD_{17}$ total score of $\geq$18.	8-week acute phase plus a double-blind extension phase for a total of 55 weeks	$HAMD_{17}$ Total Scores

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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-EW-E001; 5.3.5.4.1 (5.3.5.4.2.4); Complete; Abbreviated	Safety and Efficacy	March 1993 Complete October 1993	Single arm, noncontrolled	Duloxetine tablets: 20 mg Duloxetine: 20 mg PO QD	N = 93 (M = 31; F = 62) 38.0 years (18.4-63.8)	DSM-III-R-defined unipolar MDD	6 weeks	$HAMD_{17}$ Total Scores

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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

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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-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

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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 $HAMD_{17}$ 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

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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 Reginen	# Patients (M/F) Mean Age (Range) years	Diagnosis or Inclusion Criteria	Treatment Duration	Primary Endpoint
F1J-MC-HMCQ 5.3.5.4.4.4; 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 = 480 Randomized: N = 285 (as of 01 October 2003)	DSM-IV criteria and confirmed by the MINI. $HAMD_{17}$ total score ≥18 at Visit 1	12 weeks	Global benefit-risk assessment

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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

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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

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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-HMBO Section 5.3.5.4.2.1; Complete; Full	Safety and Efficacy	July 2001 Complete March 2002	Parallel, double-blind, placebo-controlled	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 60 mg PO BID Placebo	N = 207 (M = 23; F = 184) 49.1 years (18.8-79.7)	Met criteria for fibromyalgia as defined by the American College of Rheumatology Score of ≥4 on the Fibromyalgia Impact Questionnaire at Visits 1 and 2.	12 weeks	FIQ

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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-HMAW; Complete; Abbreviated – Acute phase; 5.3.5.1.1.1 Full – Extension phase 5.3.5.2.1	Safety and Efficacy	June 2001 Completed May 2003	Acute phase: Double-blind, randomized, parallel, placebo-controlled	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 60 mg PO BID Duloxetine: 60 mg PO QD Duloxetine: 20 mg PO QD Placebo	Acute phase: N = 457 (M = 281; F = 176) 60.1 years (22.4-88.8) Extension phase: N = 337 (M = 205; F = 132) 59.77 years (22.42-88.82)	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 month.	Acute phase: 12 weeks Extension phase: 52 weeks	Weekly mean of the 24-hour average pain severity scores recorded daily on an 11-point Likert scale

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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

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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-HMAVa Acute 5.3.5.1.1.2; Complete; Full Extension 5.3.5.4.2; Synopsis	Safety and Efficacy	October 2002 Complete August 2003	Multicenter, parallel, double-blind, randomized, placebo-controlled	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg PO QD Duloxetine: 60 mg PO BID Placebo Routine care	Planned = 330 Acute N = 334 (M = 204; F = 130) Extension N = 223 (as of 01 October 2003) ≥18 years	Pain due to bilateral diabetic neuropathy caused by Type I or II diabetes mellitus	12 weeks 52-week continuation	Reduction in average pain severity as measured by an 11-point Likert scale
F1J-MC-HMAVb; 5.3.5.4.2; Ongoing; Synopsis	Safety and Efficacy	October 2002 Ongoing	Multicenter, parallel, double-blind, randomized, placebo-controlled	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg PO QD Duloxetine: 60 mg PO BID Placebo Routine care	Planned = 330 N = 346 (as of 09 December 2003) ≥18 years	Pain due to bilateral diabetic neuropathy caused by Type I or II diabetes mellitus	12 weeks 52-week continuation	Reduction in average pain severity as measured by an 11-point Likert scale

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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 pain score (question 3) of ≥2 at Visit 2	9 weeks	BPI-question 3

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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-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 frequency	12 weeks (subjects completing trial are eligible to continue in Study SBAU)	IEF – percent change from baseline; percent change for I-QOL total score

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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-SBAV; 5.3.5.4.1 (5.3.5.4.4.2); Complete; Full	Safety and Efficacy	November 2000 Complete February 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 = 683 women 52.8 years (22.5-83.8)	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 frequency	12 weeks (subjects completing trial are eligible to continue in Study SBAW)	IEF percent change from baseline; percent change for I-QOL total score

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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-SBAX; 5.3.5.4.1 (5.3.5.4.4.3); Complete; Full	Safety and efficacy	May 2001 Complete May 2002	Double-blind, stratified, randomized, parallel, placebo-controlled, multicenter study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg PO BID Placebo	N = 458 women 53.2 years (27-79)	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 frequency.	Duloxetine: 12 weeks Placebo: 12 weeks	IEF percent change from baseline; percent change for I-QOL total score

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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 BID 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

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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-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
F1J-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

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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 F1J-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

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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-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
F1J-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

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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-SBAM; Acute phase – 5.3.5.4.1 (5.3.5.4.4.13); Complete Extension phase – 5.3.5.4.5.11; Ongoing ; Synopsis	Safety and efficacy	May 2001 Ongoing	Double-blind, stratified, randomized, parallel, placebo-controlled, multicenter study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40-60 mg PO BID Placebo	Planned = 100 women N = 109 women (as of 15 Dec 2003) 18-75 years	Subjects electing surgery for severe pure genuine stress incontinence	Active period: up to 12 weeks Open-label period: until duloxetine is commercially available for the treatment of UI or until the sponsor stops the study	Percent change in IEF from baseline to endpoint, 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

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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

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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

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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

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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-SBCC; 5.3.5.4.5.1; Ongoing; Synopsis	Safety and efficacy	July 2003 Study ongoing	Double-blind, randomized, parallel, placebo-controlled, multicenter study.	Duloxetine: 40 mg BID. Placebo	3600 women planned 437 women randomized (as of 15 Dec 2003)	Female outpatients 18 years of age with predominant SUI symptoms will participate in this study.	6 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

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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-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

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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-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, multi-center 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

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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-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	Safety--Adverse events, blood pressure, heart rate, ECGs, neurological exams, clinical laboratory tests (serum chemistry, hematology coagulation studies, urinalysis) Pharmacokinetic--Plasma 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 BID 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	Safety--Physical examination, blood pressure, pulse rate, body temperature, weight, ECG, clinical laboratory tests (hematology, urinalysis, and liver tests), adverse events. Pharmacokinetic--Standard multiple-dose pharmacokinetic parameters for duloxetine at each dose level.

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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-HMBN 5.3.5.4.1 (5.3.3.1.3); Complete; Full	Randall Stoltz, M.D./ West Pharmaceutical Services Evansville, IN/ 1 center	Open-label, dose escalation	N = 12 M = 6 F = 6 / Age 23–61	Healthy adults; Body mass index (BMI) < 35 kg/m^2	17 days/ 60 mg x 1; 60 mg QD x 8 days; 60 mg BID x 7.5 days	60-mg capsules containing duloxetine 20% w/w enteric-coated pellets	Safety--Vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinetic--Standard single- and multiple-dose pharmacokinetic parameters for duloxetine and metabolites.
F1J-LC-HMAB 5.3.5.4.1 (5.3.3.1.9); Complete; Full	D.L. Hyslop, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN/ 1 center	Single-blind, placebo-controlled	N = 9 M = 9 Ages 26-55	Healthy adults; Body mass index (BMI) < 35 kg/m^2	5 weeks	5 mg – 80 mg capsules containing duloxetine 20% w/w enteric-coated pellets	Safety—Clinical laboratory tests, nervous system examination, pupil size, blood pressure measurements, ECGs. Pharmacokinetic--Standard single- and multiple-dose pharmacokinetic parameters for duloxetine and metabolites.
F1J-LC-SAAZ 5.3.5.4.1 (5.3.3.1.1); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN/ 1 center	Open-label, single-dose	N = 4 M = 3 F = 1/ Age 37-48	Healthy adults within 30% of ideal body weight	20.2 mg single dose	20.2 mg ^{14}C-labeled (100 µCi) duloxetine enteric-coated tablet	Safety--Vital signs, ECGs, routine laboratory tests, clinical assessment, and adverse events. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine and total radioactivity. Metabolite identification Elimination pathways

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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-SBAA; 5.3.5.4.1 (5.3.3.4.4); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research/ Indianapolis, IN/ 1 center	Open-label, 4-way crossover, (fasting x 2; high fat breakfast and bedtime)	N = 14 M = 0 F = 14 / Age 18-50	Healthy adult females; within 30% of ideal body weight	4 days/ 40mg x 4 with 1 week washout between each dose	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	Safety--Vital signs, ECGs, routine laboratory tests, and adverse events. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine.
F1J-LC-BD-0001; 5.3.5.4.1 (5.3.4.1.2.); Complete	Michel Guillaume, M.D./ Aster-Cephac Paris, France/ 1 center	Randomized, double-blind, 3-period cross-over, placebo- and desipramine -controlled, evaluating 2 regimens of duloxetine	N = 12 M = 12 F = 0/ Age 23-38	Healthy adult males; extensive metabolizers with regard to CYP2D6 phenotype	7 days/ 80 mg QD x 7 days (n=6) 60 mg BID x 6.5 days (n=6); Desipramine 50 mg BID x 6.5 days Placebo x 6.5 days	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	Safety-- Electrocardiogram, laboratory tests, recording of symptoms and vital signs. Pharmacokinetic--Plasma concentration measurements of duloxetine and desipramine (No formal PK analyses performed) Pharmacodynamic--Pressor response to IV bolus injection of tyramine; 24 hour urinary catecholamines and metabolites; Whole blood 5-HT; Polygraphic sleep recordings (hypnographic EEG parameters); Leeds sleep questionnaires.

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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/ 1 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; 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-HMBG 5.3.5.4.1 (5.3.1.2.1); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN/ 1 center	Open-label, randomized 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 pellets (Commercial formulation)	Safety--Vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine. Standard bioequivalence criteria based on C_{max} and AUC.

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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).

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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	1 day/ 20 mg single dose	20-mg capsules containing duloxetine 10% w/w enteric-coated pellets	Safety--Vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinetic--Standard 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	Safety--ECGs, orthostatic blood pressure and pulse rate measurements, body weight, vital signs, clinical laboratory testing Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine and metabolites.

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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 Bioavailability 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	Safety--Vital signs (systolic and diastolic blood pressure, heart rate), ECG, clinical laboratory tests (clinical chemistry, hematology), and adverse events. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine.

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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-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 / 1 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	Safety--Safety parameters included vital signs, ECGs, clinical laboratory tests, and adverse events Pharmacokinetic--Standard multiple-dose 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/ 1 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	Safety--Safety parameters included vital signs, ECGs, clinical laboratory tests, and adverse events. Pharmacokinetic--Plasma duloxetine concentrations and blood ethanol concentrations of ethanol. (No formal PK analyses were performed) Pharmacodynamic--Measures included Alcohol Effects Scale questionnaire and Automated Performance Test System

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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	Safety--Physical examination, vital signs, ECGs, clinical laboratory evaluations. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine.

(continued)

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	Safety--Vital signs, ECGs, clinical laboratory tests, adverse events. Pharmacokinetic—Standard multiple-dose pharmacokinetic parameters for duloxetine and lorazepam. Pharmacodynamic--Immediate 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.

(continued)

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-HMBF; 5.3.5.4.1 (5.3.3.4.3); Complete; Full	Jean-Philippe Decourt, M.D./ Parexel Clinical Pharmacology Poitiers, France/ 1 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 single-dose 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	Safety--physical examination, vital signs, ECGs, clinical laboratory evaluations Pharmacokinetic—Standard multiple-dose pharmacokinetic parameters for duloxetine.

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

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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
F1J-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 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

(continued)

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-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 BID 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

(continued)

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[a]/ Regimen[b]	Duloxetine test product and strength (mg base)[c]	Criteria for Evaluation
F1J-LC-SBCG; 5.3.3.1.2; Complete; Synopsis	Dr. K. Rathgen Human Pharmacology Centre Boehringer Ingelheim Pharma GmbH & Co. KG D-88397 Biberach / Riss Clinical Research 1 Center	Randomized, placebo controlled, double blind trial.	Planned: 32 subjects (12* 40 mg; 12* 100 mg; 8* placebo) Randomized: 32 subjects Completed: 26 subjects	Healthy female subjects as determined by results of screening. Signed written informed consent in accordance with GCP and local legislation. Age ≥ 40 years . BMI ≥ 18.5 and ≤ 29.9 kg/m^2	7 days Duloxetine 20 mg capsules 40 mg or 100 mg BID po	Duloxetine to 20 mg capsules, 5 capsules twice daily or Duloxetine 20 mg 2 capsules twice daily and 3 capsules placebo twice daily given orally.	Safety: Tolerability (adverse events), ECG, systolic and diastolic blood pressure, routine labs.
F1J-LC-HMAD; 5.3.5.4.1 (5.3.3.1.6); Complete	N/A	N/A	N/A	N/A	N/A	N/A	N/A

(continued)

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

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Table 5.2. Tabular Listing of Clinical Studies (continued)

Extrinsic Factor PK Study Reports

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-HMCC; 5.3.5.4.1 (5.3.3.4.8); Complete; Full	Michael H. Skinner, M.D., Pharm.D. Lilly Laboratory for Clinical Research One	Randomized, open label 4-arm sequential treatment crossover study	14 Males 18-65 Years	4 Weeks Male Smokers	Duloxetine 60 mg orally, single dose (two occasions) Duloxetine: 10 mg intravenous solution, single dose (two occasions)	Duloxetine capsules, 20 mg Duloxetine IV, 10 mg	Drug-Drug Interaction Study

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Table 5.2. Tabular Listing of Clinical Studies (continued)

Reports of Human Pharmacodynamics (PD) 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-HMAE; 5.3.5.4.1 (5.3.4.1.3); Complete; Full	D. L. Hyslop, MD U. S. Schwertschlag, MD, PhD Lilly Laboratory for Clinical Research One	Double-blinded, randomized, three-way crossover study	N = 12 M = 12	Healthy male subjects	68 days (duloxetine 5 mg QD for 14 days; duloxetine 20 mg QD for 14 days; placebo for 40 days)	Duloxetine (low dose): 5.0 mg/day, Duloxetine (high dose): 20.0 mg/day, Placebo,	Safety
F1J-MC-SAAN; 5.3.5.4.1 (5.3.4.1.4); Complete; Abbreviated	N/A	N/A	N/A	N/A	N/A	N/A	N/A

(continued)

Table 5.2. Tabular Listing of Clinical Studies (continued)

Reports of Human Pharmacodynamics (PD) 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-HMAJ; 5.3.5.4.1 (5.3.3.4.7) Complete; Clinical Study Summary	James C. Kisicki, MD Harris Laboratories, Inc. One	single-blinded, sequential dosing	N = 12 M = 12 19-55 years	Healthy male subjects	18 days Treatment 1: One capsule of Restoril _ 30 mg and one tablet duloxetine placebo as a combination dose with 240 mL water at 11:00 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.	**Duloxetine** 20 mg Restoril 30 mg Placebo	Drug-Drug Interaction Study

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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 (5.3.5.4.6.5)
F1J-JE-301G	5.3.5.4.1 (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 (acute phase)	5.3.5.4.1 (5.3.5.4.6.9)
F1J-JE-321G (compassionate use phase)	5.3.5.4.1 (5.3.5.4.6.1)
F1J-JE-322G	5.3.5.4.1 (5.3.5.4.6.11)

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Table 5.2. Tabular Listing of Clinical Studies (concluded)

Studies Conducted By Shionogi & Co.

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 (Urge Study)	5.3.5.4.1 (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; I-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.