5.2. Tabular Listing of All Clinical Studies

Cymbalta
(duloxetine hydrochloride)
Major Depressive Disorder

Date approved by Lilly: 07 June 2005

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

Abbreviations for Table of Studies

2DCT = 2-Digit Cancellation Test
5-HT = serotonin
AE = adverse event
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 = apparent plasma clearance
Cmax = maximum plasma concentration
CMG = cystometrogram
DAI = detrusor activity index
DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, Third Edition- RevisedTM
DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth EditionTM
DTA WSS = Daily Telephone Assessment Weighted Symptom Score
ECG = electrocardiogram
F = female
HAMA = Hamilton Anxiety Rating Scale
$HAMD_{17}$ = 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
MADRS = Montgomery-Asberg Depression Rating Scale
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
PFMT = pelvic floor muscle training
PGI-Improvent = Patient's Global Impressions of Improvement
PK = pharmacokinetic
PO = orally
QD = once daily
QIDS-SR16 = Quick Inventory of Depressive Symptomatology – Self Report
SDST = Symbol Digit Substitution Test
SPT = stress pad test
SSRI = selective serotonin reuptake inhibitor
SUI = stress urinary incontinence
TEAE = treatment-emergent adverse event
Tmax = time to maximum concentration
UI = urinary incontinence
UUI = urge urinary incontinence
VLPP = Valsalva Leak Point Pressure
VLRT = Verbal Learning and Recall Test

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 (Group A); included with original submission; Complete; Full	Safety and Efficacy	February 1999 Complete May 2000	Multicenter, parallel group, double-blind, randomized placebo-controlled study with blinded placebo lead-in and lead-out	Duloxetine capsules: 10 mg and 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)	Outpatients aged 18-65 years with 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 (Group B); original submission; Complete; Full	Safety and Efficacy	March 1999 Complete January 2001	Multicenter, parallel group, double-blind, randomized placebo-controlled study with 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)	Outpatients aged 18-65 years with 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-HMAT (Group A); original submission; 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)	Outpatients ≥18 years with 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-HMAT (Group B); original submission; 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)	Outpatients ≥18 years with 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

(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-HMAY (Group A); original submission; 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)	Outpatients ≥18 years with 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-HMAY (Group B); original submission; 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)	Outpatients ≥18 years with 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

(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-HMBH (Group A); original submission; 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)	Patients ≥ 18 years with 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-HMBH (Group B); original submission; 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)	Patients ≥ 18 years with 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

(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-HMBC; 5.3.5.1.3; Complete; Full	Safety and Efficacy	March 2002 Complete July 2003	Multicenter, randomized, double-blind, placebo-controlled, parallel group study	Duloxetine capsules: 30 mg Placebo capsules Acute Therapy: Duloxetine: 60 mg PO QD Continuation Phase: Duloxetine: 60 mg PO QD Rescue Phase: Duloxetine: 60 mg PO QD 30 mg PO BID Follow-up Phase: Duloxetine: 30 mg PO QD 30 mg PO BID Placebo	N = 533 (enrolled) M = 150 F = 383 N = 278 (randomized) M = 76 F = 202 45.2 years (19.0-76.1)	Outpatients ≥ 18 years with DSM-IV–defined MDD; CGI-S score ≥4 at Visits 1 and 2 and $HAMD_{17}$ total score ≥18 at Visits 1 and 2.	38 weeks	Time to relapse during continuation phase using the log rank test.
F1J-MC-HMAU; original submission; Complete; Abbreviated	Safety and Efficacy	February 2000 Complete Oct 2001	Multicenter, long-term, open-label study	Duloxetine capsules: 20 mg Duloxetine: 40 – 60 mg PO BID	N = 1279 (M = 351; F = 928) 44.4 years (18.1-87.4)	Outpatients ≥ 18 years of age with DSM-IV–defined MDD; CGI-Severity score ≥3 at Visits 1 and 2	52 weeks	Safety: Collection and reporting of discontinuation rates, TEAEs, vital signs, ECGs and laboratory analyses.

(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-HMAG; original submission; Complete; Abbreviated	Safety and Efficacy	February 1993 Complete November 1994	Single Center, 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)	Outpatients aged ≥ 18 – 72 with DSM-III-R-defined unipolar MDD; for at least 1 month. $HAMD_{17}$ total score of ≥17 at Visit 1.	10 weeks	$HAMD_{17}$, MADRS Total Scores
F1J-MC-HMAH; original submission; Complete; Abbreviated	Safety and Efficacy	November 1993 Complete September 1995	Multicenter, double-blind, placebo-controlled, randomized, parallel design, with placebo lead-in	Duloxetine tablets: 10 mg, 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)	Outpatients aged ≥ 18 – 72 with DSM-III-R-defined MDD. $HAMD_{17}$ total score of ≥17 at Visit 1.	54 weeks	$HAMD_{17}$

(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-HMAI; original submission; Complete; Abbreviated	Safety and Efficacy	December 1993 Complete January 1996	Multicenter, randomized, parallel, double-blind, placebo- and active comparator-controlled study	Duloxetine: 5 mg, 10 mg, 20 mg tablets 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)	Inpatients or Outpatients ≥ 18 years with DSM-III-R-defined criteria for unipolar MDD. $HAMD_{17}$ total score of ≥18.	55 weeks	$HAMD_{17}$ Total Scores
F1J-EW-E001; original submission; Complete; Abbreviated	Safety	March 1993 Complete October 1993	Multicenter, single arm, noncontrolled	Duloxetine:20 mg tablets Duloxetine: 20 mg PO QD	N = 93 (M = 31; F = 62) 38.0 years (18.4-63.8)	Outpatients ≥ 18 – 65 years with DSM-III-R-defined unipolar MDD	6 weeks	Safety: Discontinuation rates, TEAEs, laboratory analyses, vital signs and ECGs.

(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-US-HMBY; not included (safety study on dose escalation); Complete; Abbreviated	Safety	Acute phase: June 2002 Complete October 2002	Multicenter, double-blind, dose escalation study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60-120 mg PO QD Placebo	N = 128 ≥18 years	Outpatients ≥ 18 years with DSM-IV-defined MDD; $HAMD_{17}$ total score ≥15 at Visits 1 and 2	7 weeks	Safety: Discontinuation rates, TEAEs, laboratory analyses, vital signs and ECGs.
F1J-US-HMBZ; Not included (no control); Completed; Abbreviated	Safety and Efficacy	Acute phase: November 2002 Complete February 2004	Multicenter, open-label, flexible dose study	Duloxetine capsules: 30 mg Duloxetine: 60-120 mg PO QD	N = 177 (Acute phase) ≥18 years	Outpatients ≥18 years with DSM-IV criteria for major depression. CGI-Severity score ≥4 at Visits 1 and 2; clinician-rated $HAMD_{17}$ total score ≥15 at Visits 1 and 2	12 weeks	Compare stabilized duloxetine dose in treatment naïve patients and SSRI switch patients.

(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-HMBV; 5.3.5.1.2; Complete; Full	Safety and Efficacy	March 2003 Complete July 2004	Multicenter, parallel, double-blind, placebo-controlled study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg PO QD Placebo	Randomized: N = 311 (M = 126; F = 185) 72.9 years (65.0 – 89.8)	Outpatients ≥ 65 years with DSM-IV criteria for MDD. $HAMD_{17}$ total score ≥18 at Visits 1 and 2. MMSE score of ≥20 with or without mild dementia.	10 Weeks	Composite cognitive score derived from the VLRT, SDST, 2DCT, and the LNST.
F1J-MC-HMCQ; Not included (no placebo control); Complete Abbreviated	Safety and Efficacy	July 2003 Complete March 2004	Multicenter, randomized, double-blind, parallel study.	Duloxetine: 30 mg capsules Venlafaxine: 75 mg capsules Duloxetine: 60 to 120 mg/day PO Venlafaxine extended release: 75 to 225 mg/day PO Placebo	Planned: N = 480 Randomized: N = 504 42 (18 – 85)	Outpatients ≥ 18 years with DSM-IV criteria for MDD and confirmed by the MINI. $HAMD_{17}$ total score ≥18 at Visit 1.	12 weeks	Global benefit-risk assessment

(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-HMBU; Not included (no placebo control); Complete; Abbreviated	Safety and Efficacy	August 2003 Complete May 2004	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 Randomized: N = 332 44 (19 – 82 years)	Outpatients ≥18 years with DSM-IV criteria for MDD and confirmed by the MINI. $HAMD_{17}$ total score ≥18 at Visit 1.	12 weeks (with possible 3-week taper period)	Global benefit-risk assessment
F1J-MC-HMCN; Not included: compassionate use; Ongoing; Abbreviated	Safety	July 2003 Ongoing	Multicenter, open-label, compassionate use study	Duloxetine: 30 mg capsules Duloxetine: 30 mg to 120 mg/day PO	No limitations on sample size	Open-label duloxetine compassionate use study for patients who have previously completed a neuroscience clinical trial in countries where it is not currently marketed.	Until duloxetine is approved for marketing in the country where this trial is taking place, or the Sponsor terminates the study.	Assess the safety of duloxetine, summarize and report spontaneous adverse events.

(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-HMBO; Section 5.3.5.1.4; 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	Randomized: N = 207 (M = 23 F =184) ≥18 years 49.1 years (18.8 – 79.6 years)	Male and female outpatients ≥18 years of age who met criteria for fibromyalgia as defined by the ACR. Presence or absence of major depression by DSM-IV criteria using the MINI. Score of ≥4 on the Fibromyalgia Impact Questionnaire (FIQ) at Visit 1 and Visit 2.	12 weeks	FIQ Pain Item and FIQ Total Score
F1J-MC-HMAW; Original submission; Complete (Acute phase); Full	Safety and Efficacy	June 2001 Completed March 2002	Multicenter, acute phase: double-blind, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 60 mg PO BID Duloxetine: 60 mg PO QD Duloxetine: 20 mg PO QD Placebo	Randomized (actual): 457 M = 281 F = 176 60.1 (22.4 – 88.8)	Male or female outpatients ≥18 years of age with 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	Weekly mean of the 24-hour average pain severity scores recorded daily on an 11-point Likert scale

(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-HMBT; not included (no placebo control/DPN); Complete (Acute phase); Abbreviated	Safety	July 2002 Complete (Acute phase)	Multicenter, open-label, parallel safety study	Duloxetine capsules: 30 mg Duloxetine 60 mg, PO QD Duloxetine 120 mg PO BID Duloxetine 120 mg PO QD	N = 449 (Randomized, acute phase) ≥18 years	Male or female outpatients ≥18 years of age with 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.	26 weeks	MNSI
F1J-MC-HMCA; 5.3.5.1.5; Complete; Full	Safety and Efficacy	November 2002 Complete October 2003	Multicenter, parallel, double-blind, placebo-controlled acute therapy study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg BID PO Duloxetine 60 mg QD PO Placebo	Randomized: N = 354 F 49.6 (20.0-79.6)	Female outpatients ≥18 years who met the criteria for primary fibromyalgia as defined by the ACR	12 weeks	BPI- average pain item

(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
H8I-MC-HQAC; 5.3.5.1.6; Complete; Abbreviated	Comparison of psychometric instruments	May 2003 Complete June 2004	Multicenter, parallel, placebo-controlled method development study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine 60 mg PO QD; Duloxetine 60 mg PO BID; Placebo	Randomized: N = 70 Mean ages: Duloxetine 60mg QD: 42 years Duloxetine 60mg BID: 34 years Placebo: 42 years Age range: 20-70 years	Male or female outpatients ≥18 years and ≤ 70 years of age with DSM-IV non-psychotic major depression of at least 4 weeks duration, with a $HAMD_{17}$ total score ≥15 and CGI-S score ≥4 at Visit 1	Approx. 4 weeks	DTA WSS
F1J-MC-HMAV (Group A); not included (DPNP study, MDD patients excluded); Complete: acute phase; Full Extension phase: Complete; Abbreviated CSR	Safety and Efficacy	October 2002 (acute) Complete August 2003 Extension phase: Complete August 2004	Multicenter, parallel, double-blind, randomized, placebo-controlled study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg PO QD Duloxetine: 60 mg PO BID Placebo Routine care	N = 334 (M = 204 F = 130) Acute phase Extension phase: N = 237 (M = 145 F = 92) 60.7 (27.6-84.3)	Male or female outpatients at least 18 years of age with a diagnosis of diabetic neuropathic pain (pain due to bilateral diabetic neuropathy caused by Type I or II diabetes mellitus) confirmed by a score of at least 3 on the Michigan Neuropathy Screening Instrument	12 weeks acute 52-week extension	Reduction in average pain severity as measured by an 11-point Likert scale

(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-HMAV (Group B); not included (DPNP study, MDD patients excluded); Complete (Acute phase) Abbreviated Extension Ongoing	Safety and Efficacy	November 2003 Complete March 2004 (Acute phase) Extension Ongoing	Multicenter, parallel, double-blind, randomized, placebo-controlled study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg PO QD Duloxetine: 60 mg PO BID Placebo Routine care	N = 348 M = 162 F = 186 (Acute phase) N = 296 Eligible for Extension phase 58.8 (20.4 – 81.9)	Male or female outpatients at least 18 years of age with a diagnosis of diabetic neuropathic pain (pain due to bilateral diabetic neuropathy caused by Type I or II diabetes mellitus) confirmed by a score of at least 3 on the Michigan Neuropathy Screening Instrument	12 weeks acute 52-week extension	Reduction in average pain severity as measured by an 11-point Likert scale
F1J-US-HMCB 5.3.5.1.1; Complete; Abbreviated	Safety and Efficacy	March 2002 Complete November 2002	Multicenter, double-blind, placebo-controlled study	Duloxetine capsules: 30 mg Placebo capsules Duloxetine: 60 mg PO QD Placebo	Randomized: N = 282 Randomized (Acute phase) ≥18 years	Male or female outpatients ≥18 years of age with a primary diagnosis of DSM-IV-defined MDD. Patients must have a $HAMD_{17}$ 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

(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-HMCM; Not included (ongoing study); Protocol	Safety and Efficacy		Multicenter, open-label study of patients diagnosed with MDD in both primary care and psychiatric care-based outpatient settings	Duloxetine capsules: 30 mg Duloxetine 60 mg PO QD	Planned: approx. 8,000 patients ≥18 years	Outpatients who meet DSM-IV diagnostic criteria for MDD	7 weeks	Outcomes as measured by the following scales: CGI-Severity; SSI; and the QIDS-SR$_{16}$
F1J-MC-HMCX; Not included (ongoing) Protocol	Safety and efficacy		Multicenter, open-label	Duloxetine 60 mg QD	Planned: approx. 8,000 patients ≥ 18 years of age	Outpatients ≥ 18 years of age with DSM-IV diagnostic criteria for MDD	7 weeks	Effectiveness in practice-based clinical settings as measured by: CGI-S, SSI, and QIDS-SR$_{16}$
F1J-MC-HMCY; Not included (ongoing study) Protocol	Safety and efficacy		Open-label, Phase 4, multicenter study of patients diagnosed with major depressive disorder in both primary care and psychiatric care-based outpatient settings	Duloxetine 60 mg QD	Planned: approx. 8,000 patients (must be at least 18 years of age)	Outpatients who meet DSM-IV diagnostic criteria for major depressive disorder	7 weeks	Outcomes as measured by the CGI-S, SSI, and QIDS-SR$_{16}$ scales

(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-US-HMCR; Not included (ongoing) Protocol	Safety and efficacy		Double-blind, randomized, multicenter, active- and placebo-controlled study (noninferiority comparison)	Duloxetine 60 mg once daily Escitalopram 10 mg once daily Placebo	Planned: 675 patients (at least 18 years of age)	Outpatients who meet DSM-IV-defined criteria for major depressive disorder	8 months	Onset of antidepressant efficacy (defined as a 20% decrease from baseline in the Maier subscale of the $HAMD_{17}$ score throughout acute treatment) for duloxetine 60 mg QD versus escitalopram 10 mg QD
F1J-MC-HMDD; Not included (ongoing) Protocol	Safety and efficacy		Randomized, multicenter study of outpatients with major depressive disorder	Duloxetine 60 to 120 mg daily	Planned randomization: approx. 940	Outpatients who meet DSM-IV criteria for major depressive disorder	12 weeks	Remission rates, defined as the proportion of patients with a $HAMD_{17}$ score ≤ 7 at endpoint

(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-HMDG; Not included (ongoing) Protocol	Tolerability and efficacy associated with switching SSRI non-responders or partial responders to duloxetine		Open-label, randomized, multicenter study	Duloxetine 60 to 120 mg daily	Planned randomization: approx. 360	Male or female outpatients at least 18 years of age who meet criteria for major depressive disorder, according to diagnostic criteria in DSM-IV	10 weeks	Noninferiority as measured by the $HAMD_{17}$ total score (mean change from baseline to endpoint)
F1J-US-HMDR; Not included (ongoing) Protocol	Safety and efficacy		Double-blind, randomized, multicenter, parallel, dose comparison study	Duloxetine 60 mg to 120 mg once daily for up to 16 weeks (initial dosing following screening will be at 30 mg QD, 60 mg QD, or 30 mg BID doses).	Planned randomization: Approx. 640	Male and female outpatients who meet criteria for major depressive disorder, as defined by DSM-IV-TR.	Up to 16 weeks	Incidence of treatment-emergent nausea for patients initially dosed at duloxetine 30 mg QD versus duloxetine 60 mg QD (acute phase). Primary objective of the extension phase is a comparison of efficacy in patients not meeting response criteria during the acute phase (for those dosed at duloxetine 60 mg QD versus duloxetine 120 mg QD).

(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-HMBR; Not included (ongoing) Protocol	Safety and efficacy		Double-blind, randomized, parallel, placebo-controlled study	Duloxetine 60 or 120 mg QD (or placebo) for approx. 9 weeks in a double-blind, acute therapy phase	Planned randomization: approx. 480 (160 per treatment group) Patients must be at least 18 years of age	Male and female outpatients presenting with generalized anxiety disorder based on disease diagnostic criteria	9 weeks (acute therapy phase)	HAMA (mean change from baseline to endpoint in anxiety symptoms)
F1J-MC-HMDT; Not included (ongoing); Abbreviated	Safety and efficacy		Double-blind, randomized, placebo-controlled study with a single-blind placebo lead-in	Duloxetine 60 to 120 mg, given once daily (or placebo) for approximately 10 weeks	Planned randomization: approx. 320 patients (160 per treatment group) Patients must be at least 18 years of age	Male and female outpatients meeting DSM-IV diagnostic criteria for generalized anxiety disorder	10 weeks (double-blind acute therapy phase)	HAMA (mean change from baseline to endpoint in anxiety symptoms)

(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-HMDU; Not included (ongoing); Abbreviated	Safety and efficacy		Double-blind, randomized, placebo- and comparator-controlled study	Duloxetine: 60-120 mg QD Comparators: Venlafaxine extended release 75 to 225 mg QD; placebo	N = approx. 480 (160 per treatment group) Patients must be at least 18 years of age	Male and female outpatients meeting DSM-IV diagnostic criteria for generalized anxiety disorder (and meeting specified disease severity criteria)	10 weeks	HAMA (mean change from baseline to endpoint in anxiety symptoms)
F1J-MC-HMDI; Not included (ongoing)	Safety and efficacy (relapse prevention)		Double-blind, placebo-controlled study	Duloxetine: Once-daily dosing (60 mg to 120 mg) compared with placebo during acute treatment of 4 to 10 weeks and continuation treatment of 22 to 24 weeks	Planned enrollment: approx. 490 (acute phase), with planned randomization of approx. 257 patients for the maintenance phase . Patients must be at least 18 years of age	Male or female patients who meet DSM-IV diagnostic criteria for recurrent major depressive disorder without psychotic features (and who have met response criteria)	Up to total of approx. 88 weeks	Time to recurrence as assessed during 52-54 weeks of maintenance treatment in patients who responded to up to 34 weeks of open-label duloxetine treatment

(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-SBBU; Not included; Complete; Full	Safety and efficacy	December 2003 Complete October 2004	Double-blind, stratified, randomized, parallel, placebo-controlled, multicenter study of a fixed dose of duloxetine compared with placebo	Duloxetine: 80 mg/day, given orally twice daily as two 20 mg capsules	Planned: 120 Randomized: 121 (61 duloxetine, 60 placebo)	Female outpatients at least 20 years of age with a predominant complaint of SUI; average of at least 1 incontinent episode per day on the screening diary; urinary diurnal frequency of eight or less per day; nocturia of two or less per day; and SUI symptoms for at least 3 months prior to study entry.	8 weeks	IEF
F1J- MC-SBAT; Original submission; 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

(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-SBAV; Original submission; 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 F 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
F1J-MC-SBAX; Original submission; Complete; Full	Safety and Efficacy	May 2001 Complete May 2002	Multicenter, double-blind, stratified, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 80 mg/day, given as 40 mg BID Placebo	N = 458 F 53.2 years (27-79)	Female outpatients at least 18 years of age with SUI, defined by a predominant complaint of SUI and all of the following: Average of at least 7 incontinent episodes per week; positive Cough Stress Test result; positive Stress Pad Test result (>2.0 g); first sensation of bladder fill (urge to void) ≥100 mL; bladder capacity >400 mL	Duloxetine: 12 weeks Placebo: 12 weeks	IEF percent change from baseline; percent change for I-QOL 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-SAAW; Original submission; Complete; Full	Safety and efficacy	June 1998 Complete September 1999	Multicenter, 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)	Females 18-65 years of age with SUI reporting ≥4 incontinent episodes per week	12 weeks	IEF
F1J-MC-SBBL; original submission; Complete; Full	Safety and efficacy	July 2001 Complete September 2003	Multicenter, double-blind, stratified, randomized, parallel, placebo-controlled pilot study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40-60 mg BID PO Placebo	N = 306 F 54.6 years (21.4-84.6)	Female outpatients at least 18 years of age with bladder over activity defined as bothersome urinary urgency or UUI for a minimum of three consecutive months	12 weeks	Measured by the micturition episodes per 24 hours as recorded in 24-hour diary.

(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-SBAF; Not included (SUI study); Ongoing; Abbreviated	Safety and efficacy	January 2002 Ongoing (as of November 2003)	Multicenter, double-blind, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg BID PO plus PFMT Placebo plus PFMT	N = 201 F (as of Nov. 2003) ≥18 - 75 years	Female outpatients between 18 and 75 years of age 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
F1J-MC-SBBA; not included; Complete; Synopsis	Safety and efficacy (health outcomes)	November 2001 Complete February 2003	Multicenter, double-blind, and single-blind, randomized, parallel, placebo-controlled study of health outcomes of duloxetine compared with placebo	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg BID PO Placebo	N = 451 F ≥18 years	Female outpatients at least 18 years of age with SUI for ≥3 months; symptoms included ≥1 accidental urine leak per week	36 weeks	I-QOL improvement

(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-SBAU; Not included (SUI study); Ongoing; Abbreviated	Safety	April 2001 Ongoing	Multicenter, open-label, single-treatment-group extension study (for those who had successfully completed Study F1J-MC-SBAT)	Duloxetine capsules: 20 mg Duloxetine: 40 mg BID PO	N = 363 F (as of October 2003)	Female outpatients with a predominant diagnosis of SUI who successfully completed Study SBAT	Until duloxetine is commercially available for the treatment of UI or sponsor stops the study	Long-term safety data
F1J-MC-SBAW; Not included (SUI study); Ongoing; Abbreviated	Safety	March 2001 Ongoing	Multicenter, open-label, single-treatment-group extension study to Study F1J-MC-SBAV	Duloxetine capsules: 20 mg Duloxetine: 40 mg BID PO	N = 493 F (as of October 2003)	Female outpatients with a predominant diagnosis of SUI who successfully completed Study SBAV	Until duloxetine is commercially available for the treatment of UI or the sponsor stops the study	Long-term safety data
F1J-MC-SBAY; Not included (SUI study); Ongoing; Abbreviated	Safety	March 2001 Ongoing	Multicenter, open-label, single-treatment-group study of the long-term safety of duloxetine	Duloxetine capsules: 20 mg, 40 mg Duloxetine: 40 mg BID PO	N = 663 F (as of Oct. 2003) ≥18 years	Female patients who had symptoms of 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

(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-SBBM; Not included (SUI study); Ongoing; Abbreviated	Safety	September 2001 Ongoing	Multicenter, open-label, single-treatment-group extension study to Study F1J-MC-SBAX	Duloxetine capsules: 20 mg, 40 mg Duloxetine: 40 mg BID PO	N = 363 F (as of Oct. 2003)	Female outpatients with a predominant clinical diagnosis of 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; Not included (SUI study); Ongoing; Abbreviated	Biomechanical effects of duloxetine	Acute therapy: October 2001 Complete August 2003 Open-label extension: Ongoing	Multicenter, double-blind, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 80 mg/day, given as 40 mg BID PO Placebo	N = 65 F (Acute phase) 51.5 (21.5-72.9 acute phase)	Female outpatients 18-75 years of age with genuine stress incontinence (normal compliance and no detrusor instability) 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	VLPP; urethral pressure measures

(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-SBAM; Not included (SUI study); Ongoing; Abbreviated	Safety and efficacy	May 2001 Ongoing	Multicenter, double-blind, stratified, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40-60 mg BID PO Placebo	N = 109 F (as of Oct. 2003)	Female outpatients 18-75 years of age with a diagnosis of pure GSI with at least 2 incontinence episodes per day	Up to 8 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
F1J-MC-SBBX Not included (SUI study); Ongoing; Abbreviated	Safety (long-term safety monitoring)	December 2002 Ongoing	Multicenter, open-label, multicountry study of women with bladder overactivity	Duloxetine capsules: 20 mg Duloxctine: 80-120 mg/day given as 40-60 mg BID	N = 72 F (as of Oct. 2003)	Females who met the diagnostic criteria for bladder overactivity (and who had successfully completed Study SBBL)	52 weeks	Long-term safety

(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-SAAA; Original submission; Complete; Abbreviated	Safety and efficacy	December 1993 Complete March 1995	Multicenter, double-blind, randomized, placebo-controlled study	Duloxetine capsules: 20 mg; Placebo Duloxetine: 20 mg QD PO Placebo	N = 92 (91 = F) Mean age: 54.5-55.9 years	Outpatients (male or female 30-80 years of age) with stress, urge, or mixed incontinence	3 weeks	CMG, voiding diary, 24-hour pad test, stress pad test, and social activity questionnaire.
F1J-MC-SAAB; Original submission; Complete; Abbreviated	Safety and efficacy	August 1995 Complete November 1996	Multicenter, double-blind, parallel, randomized, stratified, placebo-controlled study	Duloxetine capsules: 10 mg, 20 mg Placebo capsules Duloxetine 20, 30, and 40 mg/day QD PO Placebo	N = 288 F 54.8 years (22.2-78.7)	Female outpatients 18-80 years of age diagnosed with stress or mixed (with a significant stress component) urinary incontinence	6 weeks	Relationship between doses of duloxetine and efficacy as measured by change in stress pad test weight

(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-SAAH; Original submission; Complete; Synopsis	Safety and efficacy	August 1996 Complete June 1997	Singlecenter, 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)	Males and females 18 to 85 years of age with 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; Original submission; Complete; Synopsis	Safety and efficacy	April 1996 Complete August 1996	Multicenter, double-blind, placebo-controlled, randomized, parallel study	Duloxetine capsules: 10 mg, 20 mg Placebo capsules Duloxetine: 30, 40 mg/day QD PO Placebo	N = 91M 62.5 years (40.5-85.7)	Male outpatients 40 to 85 years of age with a diagnosis of mild to moderate BPH	Duloxetine: 8 weeks Placebo: 9 weeks	AUA Symptom Index 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-SAAL; Not included (original submission); 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, QD PO Oxybutynin: 7.5/10 mg/day, QD PO Placebo QD PO	N = 68 F 56.9 years (21.9-83.8)	Ambulatory, outpatient females 18 to 85 years of age with urinary frequency, urinary urgency, and nocturia	Total study time: 12 weeks (including two 4-week active treatment periods)	Efficacy as measured by BUS
F1J-MC-SBCC; Not included (SUI study); Ongoing; Abbreviated	Safety and efficacy	July 2003 Study ongoing	Multicenter, double-blind, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine: 40 mg BID PO Placebo BID	N = 86 F (as of Oct. 2003) ≥18 years	Female outpatients at least 18 years of age with predominant SUI symptoms who have an average of at least 7 incontinence episodes per week	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

(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-US-SBCD; Not included (SUI study); Ongoing; Abbreviated	Safety and efficacy	Study ongoing	Multicenter, open-label study	Duloxetine capsules: 40 mg Duloxetine 40 mg BID PO	Planned: N = 4,000 F	Ambulatory females (White, Hispanic and African-American) at least 18 years of age with incontinence episode frequency ≥7 per week who have SUI or stress-predominant mixed UI	8 weeks of active treatment	IEF
F1J-MC-SBCT; not included (SUI study); Ongoing	Study of the bio-mechanical and electro-physiological effects of duloxetine in the treatment of women with SUI	Study ongoing	Multicenter, open-label study	Duloxetine capsules: 40 mg Duloxetine 40 mg BID PO	Planned: N = 100 F 18 to 75 years	Ambulatory female outpatients 18 to 75 years of age with SUI and a positive VLPP, with discrete episodes of incontinence	Acute therapy: 4 weeks Chronic therapy: 20 weeks Discontinuation. period: 4 weeks	VLPP (change from baseline to endpoint)

(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-SBBO; Not included (SUI study); Complete; Interim full study report	Safety and efficacy	October 2003 Last patient complete: August 2004	Multicenter, double-blind, randomized, parallel, stratified, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine 40 mg BID PO Placebo given orally twice daily	N = 588 (300 duloxetine, 288 placebo) Mean 53.7 years (19.6-85.1 years)	Female outpatients at least 18 years of age with symptoms of mixed UI based on the disease diagnostic criteria; average ≥4 incontinence episodes per week on the S/UIQ; and symptoms of UI for a minimum of 3 months prior to study entry	8 weeks	IEF
F1J-MC-SBBT; Not included (SUI study); Complete; Full	Safety and efficacy	July 2003 Complete February 2005	Multicenter, double-blind, stratified, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo Duloxetine 80 mg/day (given as two 20 mg BID PO) Placebo	N = 121 F Mean 54.4 years (30.4-79.2 years)	Female outpatients ≥20 years of age 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	8 weeks	IEF (percent change from baseline to endpoint)

(continued)

Table 5.2. Tabular Listing of Clinical Studies (concluded)

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; Not included (SUI study); Ongoing; Abbreviated	Efficacy	Study ongoing (as of October 2003)	Multicenter, double-blind, randomized, parallel, placebo-controlled study	Duloxetine capsules: 20 mg Placebo capsules Duloxetine 20 mg PO BID escalating to 40 mg PO BID Duloxetine 40 mg PO QD escalating to 40 mg BID Duloxetine 40 mg BID Placebo	Planned: N = 500 F	Female outpatients at least 18 years of age with 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 Pharmacology 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-SBCH; 5.3.3.1.1 Complete; ClinPharm Study Report	Michael A. Turik, M.D., Lilly Laboratory for Clinical Research One center	Open-label dose-escalation study	N = 12 F 18 to 75 years	Healthy females 18 to 75 years of age	Total study duration: 16-20 days, depending on tolerance to drug level and ability to escalate to next higher drug level Escalating dose: Duloxetine 60 mg BID for 1-3 days; then duloxetine 120 mg BID x 1-3 days; duloxetine 160 mg BID x 4 days; duloxetine 200 mg BID x 3.5 days	Duloxetine capsules: 20 mg, 30 mg	Bioanalytical – Plasma concentrations of duloxetine were determined using a validated liquid chromatography with tandem mass spectrometry method. Pharmacokinetic – Plasma concentration versus time data for duloxetine were analyzed by noncompartmental methods. Safety – Parameters included vital signs, 12-lead ECGs, clinical lab evaluations, physical exams, and adverse event monitoring Statistical – Tabulations and descriptive statistics were used to list and summarize AEs.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMDS; 5.3.3.4.1; ClinPharm; Complete; Full	M. Turik, MD, Lilly Laboratory for Clinical Research, Indianapolis, IN; B. Laura, MD, West Pharmaceutical Services, Evansville, IN; F. Hoppcner, MD, Kendle Clinical Pharmacology Department, The Netherlands	Multicenter, open-label, multiple-dose study	N = 15 (M = 5/F = 10) 21-59 years	Health female and male subjects 21 through 59 years of age	23 days: Duloxetine 40 mg PO BID (Days 1-18), then QD (morning) on Day 19; Fluvoxaminc given 50 mg QD (evening) on Days 5-6, 100 mg on Days 7-20, 50 mg Days 21-22	Duloxetine capsules: 20 mg Fluvoxamine tablets: 50 mg	Cmax, AUC

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMAP; Original submission (not included: ClinPharm); Complete; Clinical Study Main Report	Mark J. Goldberg, M.D./ Lilly Laboratory for Clinical Research, Indianapolis, IN / 1 center	Single-blind, multiple-dose, placebo-controlled study	N = 12 M (8 males on duloxetine, 4 placebo) Age range: 22-53	Healthy adult males	21 days Duloxetine 40 mg (20 mg BID) for 7 days; duloxetine 60 mg (30 mg BID) for 7 days; and duloxetine 80 mg (40 mg BID) for 6.5 days Placebo	Duloxetine capsules: 10 mg, 20 mg Placebo capsules	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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMAR; Original submission (not included: ClinPharm) Complete; Full	Jean-Paul Macher, M.D./ Forenap Centre Hospitalier, Rouffach, France 1 center	Single-blind, randomized placebo-controlled	N = 14 M = 7 F = 7 Mean age: 31 years (23-43)	Healthy males or females 18 to 55 years of age; BMI 18 to 30	Duloxetine: 20 days Placebo: 22 days Dose escalation: Day 1-2: duloxetine 20 mg or placebo BID; Day 3-8: duloxetine 40 mg/placebo BID; Day 9-14: duloxetine 60 mg/ placebo BID; Day 15-19: duloxetine 80 mg/ placebo BID; Day 20: duloxetine 80 mg/placebo morning, placebo evening; Day 21-22: placebo BID	Duloxetine: 20 mg capsules containing enteric-coated pellets Placebo capsules	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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMBN; Not included (ClinPharm) Complete; Full	Randall Stoltz, M.D./ West Pharmaceutical Services Evansville, IN 1 center	Open-label study	N = 12 (M = 6 F = 6) Age 23–61	Healthy males or females 18-65 years; BMI < 35 kg/m^2	Approx. 17 days: duloxetine 60 mg (single dose) for 1 day; duloxetine QD 8 days; duloxetine BID 7.5 days Sequential dosing: Duloxetine 60 mg PO (single dose); duloxetine 60 mg PO QD; duloxetine 60 mg PO BID	Duloxetine: 60 mg (free base)	Safety--Vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinetic--Standard single- and multiple-dose pharmacokinetic parameters for duloxetine and metabolites.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMAB; Original submission (not included: ClinPharm) Complete; Clinical Study Summary	D.L. Hyslop, M.D./U.S. Schwertschlag, M.D., Ph.D. Lilly Laboratory for Clinical Research Indianapolis, IN/ 1 center	Single-blind, placebo-controlled study	N = 9 M = 9 Ages 26-55	Healthy males 21-55 years of age; BMI < 35 kg/m^2	5 weeks Dosage range of 5-80 mg was administered with 150-180 mL water	Duloxetine capsules: 5–80 mg (containing enteric-coated pellets) Placebo	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; Original submission (not included: ClinPharm) Complete; Full	Michael Skinner, M.D., PharmD Lilly Laboratory for Clinical Research Indianapolis, IN 1 center	Open-label, single-dose metabolic study	N = 4 M = 3 F = 1 Mean 43 years (37-48)	Healthy adults 18 to 60 years of age; within 30% of ideal body weight	Single dose	Duloxetine: 20.2mg containing approx. 100 µCi of [^{14}C]-labeled compound in an 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

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-SBAA; Original submission (not included: ClinPharm) Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research/ Indianapolis, IN/ 1 center	Open-label, randomized, 4-way crossover study	N = 14 F (1 subject DC prior to first dose) Mean age: 36 years (18-50)	Healthy females 18 to 50 years of age and within 30% of ideal body weight	Duloxetine: 4 single doses over 4 weeks 40 mg x 4 with 1 week washout between each dose	Duloxetine: 20-mg (free base) Enteric-coated capsules	Safety--Vital signs, ECGs, routine laboratory tests, and adverse events. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine.
F1J-LC-BD-0001; Not included (ClinPharm) 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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-SBBN; Original submission (not included: ClinPharm) 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) Mean age: 26 years (18-39)	Overtly healthy male and females 18 to 40 years of age	6 weeks: Duloxetine 40 mg BID PO for 2 weeks, increasing by 40 mg each week up to 240 mg daily doses (120 mg BID) Placebo	Duloxetine capsules: 20 mg free base	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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm) Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN One center	Open-label, randomized single-dose, two period, crossover study	N=26 M=6 F=20 Age 22-65	Healthy males or females 18 to 65 years of age; BMI less than 35 kg/m^2	One 60-mg capsule formulation (fasted) and a 60-mg dose (fasted) consisting of 3 x 20-mg (reference material) capsules in a randomized sequence; minimum 1-week and maximum 3-week washout period between doses	20-mg capsules containing 10% duloxetine enteric-coated pellets (clinical trial formulation) and 60-mg capsules containing 20% duloxetine enteric-coated pellets (market-designated formulation)	Safety--Vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinctic--Standard single-dose pharmacokinetic parameters for duloxetine Standard bioequivalence criteria based on C_{max} and AUC.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); Complete; Full	Michael A. Turik, M.D./ Lilly Laboratory for Clinical Research/ Indianapolis, IN 1 center	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	Duloxetine HCl: Single doses, IV and oral, on two occasions; Part A and B: approx. 30 days 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).

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMAX; Original submission (not included: ClinPharm); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN USA Robert A. Branch M.D/ Univ. of Pittsburgh Medical Center, Pittsburgh, PA/ 2 centers	Open-label, inpatient study	N = 12 (M = 10, F = 2) Mean age (healthy subjects): 46 years (24-63) Mean age (cirrhotic subjects): 44 years (20-60)	Adults 18 to 64 years of age: Those with moderate liver cirrhosis (Child-Pugh B score 7-9) and healthy subjects	1 day/ 20 mg single dose, given orally in the morning, two hours before breakfast; subjects fasted from midnight prior to dosing and for at least 2 hours after dosing	Duloxetine: 20-mg capsules	Safety--Vital signs, ECGs, clinical laboratory tests, clinical assessment and adverse events. Pharmacokinetic--Standard single-dose pharmacokinetic parameters for duloxetine and metabolites.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMBJ; Original submission (not included: ClinPharm); 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 study	N = 24 (M = 20 F = 4) End-stage renal disease subjects: Mean age: 41 years (26-55) Healthy subjects Mean age: 38.9 years (19-61)	Adults with end stage renal disease (18-70 years) requiring hemodialysis for at least 3 months; and healthy control subjects (18-75 years, age- and gender-matched) with normal renal function	Duloxetine: 60 mg single dose (3 x 20-mg capsules) after min. 3-hour fasting, between dialysis sessions	Duloxetine: 20-mg (free base) capsules	Safety--ECGs, orthostatic blood pressure and pulse rate measurements, body weight, vital signs, clinical laboratory testing Pharmacokinetic--Standard single-dose pharmacokinctic parameters for duloxetine and metabolites.
F1J-LC-SAAY; Original submission (not included: ClinPharm); Complete; Full	H. Wayne Hutman, M.D./ South Florida Bioavailability Clinic Miami, FL/ 1 center	Open-label, single-dose, inpatient, parallel group study	N = 24 F Elderly Mean age: 68.6 years (65-77) Healthy Mean age: 41.6 years (32-50)	Elderly females ≥65 years; and healthy females 18 to 50 years; within 30% of ideal body weight	40 mg single dose (2 x 20 mg capsules)	Duloxetine: 20-mg capsules	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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); Complete; Full	Michael H. Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN / 1 center	Open-label, fixed-sequence, crossover study	N = 16 M= 7 F = 9 Age range: 21-63 years	Healthy subjects 18-65 years of age with BMI less than 30 kg/m^2	Desipramine: 2 single 50-mg oral doses; Duloxetine 40 mg q12h x 6 days; Duloxetine 60 mg q12h x 15 days desipramine 50 mg alone and then with 60 mg BID duloxetine	Duloxetine: 20-mg capsules with enteric-coated pellets	Safety--Safety parameters included vital signs, ECGs, clinical laboratory tests, and adverse events
F1J-LC-HMBA; Original submission (not included: ClinPharm); Complete; Clin-Pharm Study Report	Michael Skinner, M.D./ Lilly Laboratory for Clinical Research Indianapolis, IN 1 center	Randomized, single-dose, single-blind, three-period crossover study	N = 16 M = 6 F = 10 Age 21-58	Healthy subjects 21-65 years of age with BMI less than 30 kg/m^2	Psychomotor and cognitive function measured under baseline conditions and after three single-dose treatment conditions: Ethanol plus duloxetine placebo; ethanol placebo plus duloxetine 60 mg; and ethanol plus duloxetine 60 mg	Duloxetine: 20-mg capsules	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

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); Complete; Full	Stephen D. Wise, B.Med. Sci. MB. ChB.MRCP. MFPM/ Lilly-NUS Centre for Clinical Pharmacology Pte. Ltd., Singapore/ 1 center	Open-label, randomized, 4-period crossover study	N = 14 M 24 years (21- 38)	Healthy males or females 21 to 50 years of age with BMI 19-30 kg/m^2	4 single doses of 40 mg duloxetine (2 x 20 mg) in the presence and absence of famotidine, an antacid (Mylanta), and activated charcoal. There were four randomized sequences of administration.	Duloxetine capsules: 20 mg	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 Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); Complete; Full	J. P. Macher, M.D./ Forenap Centre Hospitalier, Rouffach, France/ 1 center	Randomized double-blind, balanced, two-period, cross-over study	N = 16 M = 8 F = 8 Mean age: M = 32.3 years (26-44) F = 32.9 (21-45)	Healthy male and females 18 to 55 years of age	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 Placebo Lorazepam: 2 mg P.O. BID	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 Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); 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; Original submission (not included: ClinPharm); 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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); Complete; Abbreviated	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.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); 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 Pharmacology Studies (continued)

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-HMCG; 5.3.4.1.1; Complete; Full	D. Hoelscher, M.D. PPD Development, Austin, TX USA B. Laura, M.D., West Pharmaceutical Services (GFI), Evansville, IN USA P. Leese, M.D., Quintiles, Lenexa, KS USA et al Six study centers	Randomized, double-blind, two-way crossover study with positive control	Enrolled: 117 F 18-75 years	Healthy female subjects 18-75 years	Total duration for each study arm was up to 51 days. Following a baseline day, duloxetine and placebo were administered twice daily in two separate periods of up to 22 days each, and moxifloxacin was given as a single dose. A washout period followed.	Duloxetine 60 mg, 120 mg, 160 mg, and 200 mg given orally, twice daily (as 20 mg capsules and 30 mg capsules)	Safety – Vital signs, body weight, 12-lead ECGs, clinical lab evaluations, physical exams, psychiatric evaluation, and AE monitoring. Pharmacokinetic – Plasma concentrations of duloxetine and its two major metabolites. Pharmacodynamic – Four replicate 12-lead ECG QT interval measurements obtained at each of four time points on a baseline day and on the fourth day of dosing of both duloxetine and placebo at the two highest dose levels, and 2 and 6 hours after dosing with moxifloxacin.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Not included (ClinPharm); Complete; ClinPharm Study Report	D.L. Hyslop, M.D. U.S. Schwertschlag, M.D., Ph.D. Lilly Laboratory for Clinical Research One center	Open-label metabolic study	N = 4 M = 4	Healthy subjects	1 day.	Duloxetine 20 mg/day (given one time)	Safety, including vital signs and clinical lab tests

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-BI-SBCG; Not included (ClinPharm); Complete; Abbreviated	Dr. K. Rathgen Human Pharmacology Centre Boehringer Ingelheim Pharma GmbH & Co. KG D-88397 Biberach / Riss Clinical Research One center	Randomized, placebo controlled, double blind trial	N = 32 (planned): 12 dosed at 40 mg, 12 at 100 mg, and 8 placebo 32 randomized26 completed	Healthy female subjects ≥ 40 years. BMI ≥ 18.5 and ≤ 29.9 kg/m^2	7 days Duloxetine 40 mg or 100 mg BID	Duloxetine 20 mg capsules (5 capsules twice daily or 2 capsules twice daily) and 3 capsules placebo twice daily given orally.	Safety: Tolerability (adverse events), ECG, systolic and diastolic blood pressure, routine labs.

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMAD; Original submission (not included: ClinPharm); Complete; Clin-Pharm. Study Report	L. Hyslop, M.D. U.S. Schwertschlag, M.D., Ph.D. Lilly Laboratory for Clinical Research One	Single-blind, placebo-controlled, parallel design	N = 25 M = 25	Healthy male subjects	14-day courses of placebo or duloxetine (2.5, 5, 10, 20, or 40 mg)	Duloxetine oral, enteric-coated in the following dose strengths: 2.5 mg/day, 5 mg/day, 10 mg/day, 20 mg/day, 40 mg/day	Safety (including vital signs, ECG, and clinical lab tests)
F1J-LC-HMAA; Original submission (not included: ClinPharm); Complete; Synopsis	U.S. Schwertschlag, M.D., Ph.D., et al Lilly Laboratory for Clinical Research One	Single-blind, placebo-controlled (dose escalation study)	N = 3 M = 3 21-55 years	Healthy adult males	Single dose	Duloxetine 5-mg capsules 10-mg capsules 25-mg capsules Placebo	Safety, Pharmacokinetics, drug metabolism, and pharmaco-dynamics

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-SBAZ; Not included (PK-SUI) Complete; Full Study Report	Alan G Moskwa, MD CMAX, a Division of Institute of Drug Technology Australia Limited One	A two-part study involving single-dose duloxetine administration, conducted in a randomized, three-period crossover design and a multiple dosing period. Study evaluated 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
F1J-LC-HMCC; Original submission (not included: ClinPharm); Complete; Synopsis	Michael H. Skinner, M.D., Pharm.D. Lilly Laboratory for Clinical Research One	Randomized, open label 4-arm sequential treatment crossover study	N = 16 (all males) 18-65 Years	Healthy male smokers	4 weeks 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

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); 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; Not included (ClinPharm); Complete; Abbreviated	Julie E. Turcotte, M.D.; Guy Debonnel, M.D.; Claude de Montigny, M.D., Ph.D.; Chantal Hebert, R.N.; and Pierre Blier, M.D., Ph.D.	Double-blinded (only for duloxetine and placebo arms)	N = 27 M = 27	Healthy male subjects without history of psychiatric disorder	Fourteen (14) days, with assessment conducted at baseline, Day 7 and Day 14	Duloxetine 20 mg/day Duloxetine 60 mg/day (Comparators: clomipramine 100 mg/day, placebo)	Effects of duloxetine on serotonin and norepinephrine reuptake

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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; Original submission (not included: ClinPharm); 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

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (continued)

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-HMCE; not included (ClinPharm); Complete; Clin-Pharm/ Exploratory Study Report	Dr. Stephen D. Wise Lilly-NUS Centre for Clinical Pharmacology Pte Ltd. One	Open-label, randomized, single-dose, two-period, crossover study	N = 24 21-60 years	Healthy men and women within range of Body Mass Index 18.5-29.9 kg/m^2	Single dose of the reference and test lots in a randomized sequence, with approximately 1 week between the doses	Duloxetine (given orally as single 60 mg capsule)	Bio-equivalence of duloxetine capsules produced at two sites
F1J-LC-SBCR; Not included (ClinPharm); Complete; Clinical Pharmacol. Study Report	Michael A. Turik, MD Lilly Laboratory for Clinical Research One	Subject-blind, randomized, two-way balanced crossover study	N = 58 F = 58 18-65 years	Healthy, nonsmoking female subjects 18-65 years	Duloxetine twice daily (BID) for 4-1/2 days	Duloxetine 60 mg BID (given as three 20mg capsules)	Drug-Drug Interaction Study

(continued)

Table 5.2. Tabular Listing of Clinical Pharmacology Studies (concluded)

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-SBCS; Not included (ClinPharm); ongoing; N/A	Dr. Chris Mills Phase 1 Clinical Trials Unit, Old Convent of Notre Dame	Open-label, multiple-dose study	N = 6 (planned)	Lactating women who are weaning their infants and are willing to discontinue nursing during and after study evaluation	Duloxetine 40 mg twice daily (at 12-hour intervals) for 3 days, followed by a final dose of duloxetine 40 mg on Day Four	Duloxetine 40 mg BID (given as two 20 mg capsules)	Pharmaco-kinetics of duloxetine in plasma and breast milk of lactating women
F1J-LC-HMEE; not included (ClinPharm); ongoing N/A		Double-blind, randomized, placebo-controlled, single-period study	N ≥18 (number planned for duloxetine completion)	Healthy Chinese subjects	Single dose of duloxetine 60 mg (given as two 30 mg capsules) on Day 1, followed by duloxetine 60 mg QD for 6 days	Duloxetine 60 mg (two 30 mg capsules)	Pharmaco-kinetics of duloxetine in healthy Chinese subjects

Table 5.2. Tabular Listing of Clinical Studies (Studies Conducted by Shionogi & Co.)

Study	Location	Study	Location
F1J-JE-102G	Included in original submission (not included here)	F1J-JE-321G (compassionate use phase)	Original submission
F1J-JE-221G	Original submission	F1J-JE-322G	Original submission
F1J-JE-301G	Original submission	F1J-JE-323G	Original submission
F1J-JE-311G	Original submission	F1J-JE-324G	Original submission
F1J-JE-312G	Original submission	F1J-JE-401G (Urge Study)	Original submission
F1J-JE-313G	Original submission	F1J-JE-1008	Original submission
F1J-JE-321G (acute phase)	Original submission	F1J-JE-1009	Original submission