

All Serious Non-Fatal Adverse Experiences Reported up to Cut-off Date of 1/31/95
For the Phase II/III Pramipexole Studies

Appendix 4.11.1

Body System Body	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from		Adverse Event Verbatim	COSTART Term
						First Dose to AE Onset (days)	AE Onset (days)		
M27300001			67	Male	0		208	ALLERGIC REACTION	ALLERG REACT
			59	Male	0		120	CHEST PRESSURE/PAIN	PAIN CHEST
			41	Male	0		153	CHEST PAIN	PAIN CHEST
			61	Male	4.5		102	CHEST PAIN	PAIN CHEST
			73	Male	>		255	CHEST PAIN	PAIN CHEST
				Male	>		259	LOW BACK PAIN	PAIN BACK
				Male	>		259	MALAISE	MALAISE
			56	Female	4.5		178	CHEST PAIN	PAIN CHEST
			69	Male	0		14	INCREASED WEAKNESS	ASTHENIA
			72	Male	-		325	CHEST PAIN	PAIN CHEST
M27300002			60	Male	-		-	BACK PAIN	PAIN BACK
			75	Male	-		240	CONCUSSION	INJURY ACCID
				Male	-		241	FEVER	FEVER
			68	Female	-		28	BROKEN ANKLE	INJURY ACCID
			64	Male	-		-	NAEVUS R PARIETAL AREA	ANOMALY CONGEN
			64	Male	-		238	SWELLING ALL OVER	EDEMA GENERAL
			69	Male	-		2	BACK STRAIN/PAIN	INJURY ACCID
				Male	-		2	RIB CONTUSIONS	INJURY ACCID
				Male	-		2	ROLLOVER MOTOR VEHICLE ACCIDENT	INJURY ACCID
			79	Male	-		126	CHEST PAIN	PAIN CHEST
M27300004			70	Male	6		36	FRACTURE RIGHT HIP	INJURY ACCID
			70	Male	4.5		30	FRACTURED RIGHT HIP	INJURY ACCID
M27300006			69	Male	-	-	25	TRAUMATIC BURN TRAUMATIC BURN ON THORAX, HANDS, FACE	INJURY ACCID INJURY ACCID
M27300010			70	Female	3.75		119	FALL-R WRIST FX	INJURY ACCID
			57	Male	0.75		14	NECK PAIN	PAIN NECK
				Male	0.75		14	NECK PAIN RADIATING IN L ARM	PAIN NECK
			71	Female	0		113	BROKEN HIP	INJURY ACCID
			73	Male	-		74	FALL	INJURY ACCID
				Male	-		74	FALL IN HOME FRACTURED RIBS X3	INJURY ACCID
			56	Male	4.5		58	DEEP LACERATION PIP JOINT LT	INJURY ACCID
				Male	4.5		66	INDEX FINGER	INJURY ACCID
			54	Male	0		66	L LEG PAIN	PAIN
			69	Male	4.5		158	BACK PAIN RADIATING TO LEFT EXTREMITY	PAIN BACK
				Male	4.5		158	BK PN RAD TO LFT EXTR WITH LFT FT WEAKNESS	PAIN BACK
			59	Male	0		80	BACK PAIN	PAIN BACK
				Male	0		198	CHEST PAIN	PAIN CHEST
				Male	0		138	GROIN PAIN	PAIN
			46	Male	0		60	CELLULITIS RLE	CELLULITIS

Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from First Dose to AE Onset (days)	Adverse Event Verbatim	COSTART Term
Body	M27300010		60	Male	-	223	ABDOMINAL PAIN	PAIN ABDO
			66	Male	0	49	BACKPAIN	PAIN BACK
			59	Male	0	44	HERNIA RT INGUINAL	HERNIA
					0	44	HERNIA, RT INGUINAL	HERNIA
			63	Male	0	43	CHEST PAIN	PAIN CHEST
			62	Male	-	109	ACCIDENT	INJURY ACCID
			75	Male	-	230	FALL	INJURY ACCID
			57	Male	-	66	INFECTION AT SURGICAL WOUND	INFECT
					-	-3	INGUINAL HERNIA	HERNIA
	M27300011		65	Female	-	37	FALL	INJURY ACCID
			67	Male	-	124	FALL	INJURY ACCID
			63	Female	-	41	FRACTURE RIGHT FOREARM	INJURY ACCID
			65	Female	-	167	OVERDOSE	OVERDOSE
			69	Male	-	176	BACK PAIN	PAIN BACK
			69	Male	-	104	FALL	INJURY ACCID
			74	Male	-	178	CHEST PAIN	PAIN CHEST
			77	Male	-	5	CHEST PAIN	PAIN CHEST
			60	Female	-	113	BROKE LEFT ARM	INJURY ACCID
	M27300013		74	Male	-	89	FALL	INJURY ACCID
			53	Male	-	-	LUMBAGO	PAIN BACK
			59	Male	-	281	SEVERE CHEST PAIN	PAIN CHEST
			64	Male	-	-	BACK PAIN	PAIN BACK
			64	Female	-	-	PAINS IN THE LEFT INGUINAL	PAIN ABDO
							REGION	
			75	Female	-	624	FRACT. COLLI FEM. DXT	INJURY ACCID
			59	Female	-	624	FRACT. COLLISI DXT	INJURY ACCID
					-	38	INTRA-ARTICULAR	INJURY ACCID
	M27300014				-		RADIUS-FRACTURE TROCHANTER	
					-		MAJOR	
					-	19	INTRAARTIKUL. FRACTURE DISTAL	INJURY ACCID
					-		RADIUS LEFT 200792	
			54	Male	-	-	PAIN IN THE BACK	PAIN BACK
			74	Female	-	204	FEVER	FEVER
					-	214	PAIN	PAIN
			69	Female	-	802	ACCIDENT HOUSEHOLD*	INJURY ACCID
					-	747	PAIN	PAIN
			59	Female	-	282	PAIN	PAIN
	M27300016				-			
			67	Male	-	119	CHEST PAIN	PAIN CHEST
			76	Male	-	106	BRACHIAL PLEXUS INJURY LEFT	INJURY ACCID
					-		ARM	
					-	-	CELLULITIS R LEG	CELLULITIS
					-	97	CELLULITIS RIGHT LEG	CELLULITIS
			74	Female	-	254	PERIPELVIC CYST ON SKIN	CYST
					-			
					-			
					-			

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Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from First Dose to		Adverse Event Verbatim	COSTART Term
						AE Onset (days)			
Body	M27300018		68	Male	0	17		CHEST TIGHTNESS	PAIN CHEST
	M27300024		39	Male	-	12		ATTEMPT OF SUICIDE BY STRANGULATION	SUICIDE ATTEMPT
Cardiovascular			37	Male	-	2		ATTEMPT OF SUICIDE	SUICIDE ATTEMPT
			41	Female	-	30		SUICIDE ATTEMPT†	SUICIDE ATTEMPT
			54	Female	-	8		BP COLLAPSED	SHOCK
	M27300001		75	Male	0	89		ATRIAL FLUTTER	FLUTTER ATR
			59	Male	0	120		CORONARY ARTERY DISEASE	CORONARY ART DIS
					0	120		SINUS ARRHYTHMIA	ARRHYTHMIA ATR
					0	120		UNSTABLE ANGINA	ANGINA PECTORIS
			67	Male	0	10		ATRIAL FIBRILLATION	FIBRILLAT ATR
					0	10		INTERMITTENT TACHYCARDIA	TACHYCARDIA
			72	Male	0	183		DEEP VEIN THROMBOSIS	THROMBOPHLEB DEEP
			77	Female	4.5	114		ACUTE MYOCARDIAL INFARCT	INFARCT MYOCARD
			59	Male	0	202		BRADYCARDIA	BRADYCARDIA
					0	202		HYPOENSION	HYOTENS
	M27300002		67	Male	-	94		ATRIAL FIB.	FIBRILLAT ATR
			72	Male	-	30		ABDOMINAL AORTIC ANEURYSM	ANOMALY VASCUL
			59	Male	-	-		CORONARY ARTERY DISEASE	CORONARY ART DIS
			68	Male	-	214		ANGINA	ANGINA PECTORIS
			75	Male	-	241		ATRIAL FIBRILLATION	FIBRILLAT ATR
					-	241		IRREGULAR HEART RATE	ARRHYTHMIA
			60	Female	-	118		ANGINA	ANGINA PECTORIS
			64	Male	-	238		CONGESTIVE HEART FAILURE	HEART FAIL
			79	Male	-	126		ATRIAL FIBRILLATION	FIBRILLAT ATR
	M27300004		77	Male	4.5	36		LEFT VENTRICULAR DYSFUNCTION	HEART FAIL LEFT
			60	Male	0	9		MYOCARDIAL INFARCTION	INFARCT MYOCARD
			70	Male	6	42		BILATERAL PULMONARY EMBOLUS	EMB PULM
	M27300010		63	Male	0	43		PALPITATIONS	PALPITAT
			75	Female	0	21		SYNCOPE X2	SYNCOPE
	M27300011		67	Female	-	77		LEFT PONTIVE INFARCT	CEREBROVASC ACCID
			66	Male	-	190		DVT	THROMBOPHLEB DEEP
			74	Male	-	178		ATRIAL FIB	FIBRILLAT ATR
	M27300013		70	Male	-	50		ATRIAL FIBRILLATION	ARRHYTHMIA ATR
			53	Male	-	33		LIPOTHYMIA	SYNCOPE
	M27300014		59	Male	-	270		SEVERE M.I.	INFARCT MYOCARD
					-	566		UNSTABLE ANGINA	ANGINA PECTORIS
			65	Male	-	150		ARRHYTHMIA	ARRHYTHMIA
					-	-		MYOCARDIAL DECOMPENSATION	HEART FAIL
					-	170		TACHYCARDIA	HEART FAIL
					-	-		EMBOLISM CEREBRAL	TACHYCARDIA
			63	Male	-	664		HEART BLOCK AV	EMB CEREBR
					-	665		INTERMITTENT AURICULAR	AV BLOCK
					-	662		FLUTTER WITH 2:1 VENTRICULAR ACTIVATION	ARRHYTHMIA ATR

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Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from First Dose to AE Onset (days)	Adverse Event Verbatim	COSTART Term
Cardiovascular	M27300014	53	63	Male	-	662	INTERMITTENT AURICULAR FLUTTER WITH 2:1-VENTRICULAR ACTIVATION	ARRHYTHMIA ATR
		71	Female	-	-	665	SUSPICION OF AV-BLOCK 2.3 DEGREE UNDER THERAPY WITH ISOPTIN AND DIGOXIN	AV BLOCK
		69	Female	-	-	182	MYOCARDIAL INFARCTION	INFARCT MYOCARD
	M27300015	70	Male	-	-	-	ANGINA PECTORIS	ANGINA PECTORIS
		52	Male	1.5	28	MB. CARDIS INCOMP	HEART FAIL	HEART FAIL
	M27300016	67	Male	-	119	MYOCARDIAL INFARCTION	INFARCT MYOCARD	INFARCT MYOCARD
		69	Male	-	10	MYOCARDIAL INFARCTION	INFARCT MYOCARD	INFARCT MYOCARD
	M27300018	68	Male	0	17	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		73	Male	0	17	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300019	65	Male	5	43	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
Digestive	M27300020	67	Male	4.5	75	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		70	Female	+	-	75	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300022	54	Female	-	8	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		69	Male	>	236	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300024	50	Female	0	69	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		73	Male	>	90	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300001	69	Male	0	259	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		70	Female	+	15	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300010	70	Female	3.75	119	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		55	Male	0	87	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300011	74	Male	0	51	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		60	Male	-	223	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300018	81	Male	0	101	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		63	Male	0	101	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300011	69	Male	0	53	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		57	Male	-	157	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300018	60	Male	<	-10	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		60	Male	<	-10	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
	M27300011	60	Male	<	-10	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION
		60	Male	<	-10	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION	MYOCARDIAL INFARCTION

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Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from First Dose to AE Onset (days)	Adverse Event Verbatim	COSTART Term
Endocrine	M27300001	45	Female	1.5	72	72	THYROID NODULE +	NEOPL THYR
	M27300004	72	Male	4.5	40	40	DECREASED PLATELETS	THROMBOCYTOPENIA
	M27300010	77	Male	3.75	118	118	LUMBAR RADICULOPATHY (MULTIPLE MYELOMA)	MYELOMA
Metabolic and Nutritional	M27300001	73	Male	>	255	255	WEIGHT LOSS	WEIGHT DEC
		69	Male	0	16	16	DECREASED POTASSIUM	HYPOKALEM
	M27300002	75	Male	-	241	241	DEHYDRATION	DEHYDRAT
				-	241	241	ELEVATED CPK	CREATINE PK INC
	M27300010	49	Male	-	22	22	ELEVATED CPK	CREATINE PK INC
Musculo-Skeletal				-	22	22	HOSPITALIZATION DUE TO ELEVATED CK(CPK)	CREATINE PK INC
	M27300020	58	Male	4.5	47	47	ELEVATED SERUM CK	CREATINE PK INC
	M27300002	60	Male	-	177	177	MRSA INFECTION OF T10-T11,T12	OSTEOMYELITIS
	M27300010	69	Male	4.5	158	158	LEFT FOOT WEAKNESS	MYASTHENIA
	M27300011	67	Female	-	229	229	INCREASED RT SIDE WEAKNESS	MYASTHENIA
		77	Female	-	-75	-75	ARTHRITIC PAIN(SPINAL STENOSIS)	ARTHRITIS
	M27300014	63	Male	-	-	-	OSTEOPOROSIS	OSTEOPOROSIS
		62	Male	-	-	-	DEG. MENISKOPATH	JOINT DIS

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ON ORIGINAL

Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from First Dose to AE Onset (days)	Adverse Event	COSTART Term
Nervous	M27300001		59	Male	0.75	14	DROWSINESS	SOMNOLENCE
			59	Male	1.5	16	DROWSINESS	SOMNOLENCE
			59	Male	0	202	DIZZINESS	DIZZINESS
			69	Male	0	202	LIGHTHEADEDNESS	DIZZINESS
	M27300002		69	Male	0	14	WORSENING PARKINSON'S DISEASE	EXTRAPYR SYND
			67	Male	-	93	ACUTE SEIZURE ACTIVITY	CONVULS
			65	Male	-	70	INCREASED VISUAL HALLUCINATION	HALLUCIN
			65	Male	-	70	WORSENING OF PARKINSON'S DISEASE	EXTRAPYR SYND
			67	Male	-	95	LEFT HEMISPHERIC INFARCT (INSULAR CORTEX)	INFARCT CEREBR
			62	Female	3	28	SEVERE SOMNOLENCE RAN OFF ROAD IN HER CAR	SOMNOLENCE
	M27300010		71	Male	1.5	61	CONFUSION	CONFUS
			71	Male	1.5	61	HALLUCINATIONS	HALLUCIN
			65	Male	+	-	NUMB TINGL ACHE WEAK (CER RADICULOPATHY)	NEUROPATHY
			68	Female	-	15	PARANOIA	PARANOID REACT
			71	Female	-	15	VISUAL HALLUCINATIONS	HALLUCIN
			75	Female	0	113	DIZZINESS	DIZZINESS
			75	Female	0	51	CONFUSION	CONFUS
			74	Male	0	51	PARANOIA	PARANOID REACT
			75	Male	4.5	123	INCREASED OFF PERIODS	EXTRAPYR SYND
			75	Male	0	108	RIGHT CEREBRAL INFARCT (BET 7-15-94 + 7-22-94)	INFARCT CEREBR
	M27300011		72	Male	0.75	74	CONFUSION	CONFUS
			75	Male	-	136	PSYCHOSIS	PSYCHOSIS
			36	Male	-	106	TIA	ISCHEMIA CEREBR
			65	Female	-	5	AKINETIC	AKINESIA
			71	Male	-	101	INCR DYSKINESIAS	DYSKINESIA
			71	Male	-	119	CONFUSION	CONFUS
	M27300013		52	Male	-	-6	PARANOIA	PARANOID REACT
			79	Female	-	-	INCREASE OF PARKINSON SYNDR.	EXTRAPYR SYND
			-	-	-	-	INCREASE OF PARKINSON SYNDROM	EXTRAPYR SYND
			-	-	-	1	INCREASE OF PARKINSON SYNDROMS	EXTRAPYR SYND
	M27300014		63	Female	-	999	AGGRAVATION OF PARKINSON'S SYMPTOMS	EXTRAPYR SYND
			72	Male	-	460	AGGRAVATION OF PARKINSON'S SYMPTOMS	EXTRAPYR SYND
			64	Male	-	207	PAINFUL DYSKINESIA	DYSKINESIA
			55	Female	-	2	DIZZINESS, NAUSEA FAINTING	DIZZINESS
			-	-	-	-	-	-

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Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from First Dose to AE Onset (days)	Adverse Event Verbatim	COSTART Term
Nervous	M27300014	59	Male	-	-	-	PARKINSONISM AGGRAVATED	EXTRAPYR SYND
		65	Male	-	150	-	PARKINSONISM AGGRAVATED	EXTRAPYR SYND
		54	Female	-	337	-	INCREASED PARKINSONISM	EXTRAPYR SYND
		50	Male	-	106	-	ANXIETY	EXTRAPYR SYND
		74	Female	-	32	-	WORSENING OF PARKINSON	EXTRAPYR SYND
		52	Male	-	597	-	LUMBAR NERVE ROOT COMPRESSION	NEURALGIA
				-	597	-	RELAPSE OF	NEURALGIA
		70	Male	-	-	-	HALLUCINATIONS	HALLUCIN
				-	-	-	SEVERE "OFF-PERIODS"	EXTRAPYR SYND
		74	Female	-	-	-	LONG AND PAINFUL OFF-PERIODS, INNER RESTLESS	EXTRAPYR SYND
	M27300015	35	Male	+	1.5	-	ACUT PSYCHOTIC SYMPTOMS	SCHIZOPHRENIC REACT
				-	-	-	EXAC. OF PSYCHOSIS WITH HALLUCIN.	SCHIZOPHRENIC REACT
				2	33	-	REHOSPITALIZ. BEC. OF PRAEPSY. SIGNS	SCHIZOPHRENIC REACT
		53	Male	+	-	-	REHOSPITALISATION	SCHIZOPHRENIC REACT
		49	Female	+	34	-	EXACERBATION OF PSYCHOSIS	SCHIZOPHRENIC REACT
				-	-	-	INCREASED HALLUCINATORY BEHAVIOR	HALLUCIN
				+	-	-	RESTLESSNESS, AGRESSIVITY	HOSTILITY
		74	Female	-	32	-	NEUROPATHY	NEUROPATHY
		48	Male	<	-21	-	DYSTONIA	DYSTONIA
				<	-20	-	SEVERE OFF PERIOD (WORSENING OF DISEASE)	EXTRAPYR SYND
	M27300019	47	Male	+	0	-	INCREASE OF BLOCKAGES	EXTRAPYR SYND
				+	59	-	INCREASING OFF PERIODS	EXTRAPYR SYND
				-	-	-	WORSENING OF PARKINSON. -BLOCKAG.	EXTRAPYR SYND
		67	Male	1.5	18	-	FALL WITH	GAIT ABNORM
		58	Male	4.5	45	-	(R) HUMERUS	CONFUS
				4.5	45	-	CONFUSION	SONNOLENCE
				-	58	-	HYPERSOMNOLENCE	HALLUCIN
		54	Male	-	36	-	HALLUCINATION (VISUAL/AUDITORY)	PSYCHOSIS
		72	Male	-	37	-	PARANOID PSYCHOSIS	DYSKINESIA
		62	Female	2	-1	-	DYSKINESIA	AGITATION
	M27300024	37	Male	-	-	-	ACUTE ANGUISH	
				-	-	-		
				-	-	-		
				-	-	-		
				-	-	-		
				-	-	-		
				-	-	-		
				-	-	-		
				-	-	-		
				-	-	-		
Nervous	M27300024	39	Male	-	40	-	EPILEPTIC CRISES	CONVULS
		41	Female	-	25	-	STATE OF DEPRESSION	DEPRESSION

Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from		Adverse Event	COSTART Term
						First Dose to	AE Onset (days)		
Respiratory	M27300001		42	Female	>		126	BILATERAL PNEUMONIA	PNEUMONIA
							106	R MIDDLE LOBE PNEUMONIA	PNEUMONIA
	M27300002		77	Male	-		164	SHORTNESS OF BREATH	DYSPNEA
	M27300004		77	Male	3		32	DYSPNEA	DYSPNEA
	M27300010		72	Male	3		30	PNEUMONIA	PNEUMONIA
			72	Male	0.75		71	PNEUMONIA	PNEUMONIA
	M27300011		71	Male	-		33	DYSPNEA	DYSPNEA
	M27300014		67	Male	-		6	PNEUMONIA	PNEUMONIA
			63	Male	-		-	BRONCHITIS	BRONCHITIS
					-		-	DYSPNEA	DYSPNEA
			65	Male	-		-	TACHYPNOEA	HYPERVENTIL
			63	Male	-		657	EXACERB. COPD WITH BRONCHIAL SUPERINFECTION	EMPHYSEMA
			73	Male	-		443	EXACERB. COPD WITH BRONCHITIS	EMPHYSEMA
			70	Male	-		575	DYSPNOE	DYSPNEA
					-		463	OEDEMA PULMONIUM	EDEMA LUNG
			67	Female	4		71	ACUTE PNEUMONIA	PNEUMONIA
Skin	M27300001		70	Male	0.375		1	BASAL CELL CARCINOMA OF L EAR	CARCINOMA SKIN
			78	Female	0		106	SKIN CANCER-LEFT CHEEK	CARCINOMA SKIN
	M27300002		78	Female	-		-	SKIN CANCER-LEFT CHEEK	CARCINOMA SKIN
			73	Male	-		191	MELANOMA	MELANOMA SKIN
	M27300014		59	Male	-		0	EXCISION OF MELANOMA (R) FLANK, (L) THIGH	MELANOMA SKIN
Special Senses		M27300014	42	Female	-		-	BLEPHAROSPASM	EYE DIS

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Body System	Study Number	Patient Number	Age	Gender	Dose mg/day	Time from		Adverse Event	COSTART Term
						First Dose to	AE Onset (days)		
Urogenital	M27300001		70	Male	4.5	-	222	PROSTATE CANCER	CARCINOMA PROSTATE
			72	Male	0	-	174	ADVANCED BLADDER TRABECULAE	UG DIS
					0	-	197	BLADDER CANCER	CARCINOMA BLADDER
					+	-	-	CYSTITIS	CYSTITIS
					+	-	-	OBSTRUCTED PROSTATE	PROSTAT DIS
	M27300002		61	Male	4.5	-	215	CA OF PROSTATE	CARCINOMA PROSTATE
			67	Male	-	-	70	WORSENING BPH	PROSTAT DIS
			70	Male	-	-	-	PROSTATE CANCER	CARCINOMA PROSTATE
			61	Male	-	-	-	CA OF PROSTATE	CARCINOMA PROSTATE
	M27300004		68	Female	+	-	-	BREAST MALIGNANT NEOPLASM, FEMALE	CARCINOMA BREAST
	M27300010		75	Male	0	-	83	ABNORMAL URINE COLOR	URIN ABNORM
			72	Male	>	-	101	ACUTE URINARY RETENTION	URIN RETENT
	M27300011					-	32	MASS R KIDNEY	CARCINOMA BLADDER
			68	Male	-	-	28	UTI	INFECT URIN TRACT
			57	Male	-	-	97	ACUTE URINARY RETENTION	URIN RETENT
			66	Male	-	-	209	HEMATURIA	HEMATURIA
			77	Male	-	-	62	HEMATURIA	HEMATURIA
	M27300014		71	Male	-	-	-	PROSTATIC CARCINOMA*	CARCINOMA PROSTATE
			63	Male	-	-	463	PROSTATE CANCER	CARCINOMA PROSTATE
			46	Male	-	-	-	SPASTIC BLADDER / INCONTINENS	INCONTIN URIN
			66	Male	-	-	53	HYDROCELE	EPIDIDYMITIS
	M27300016		43	Female	-	-	125	FIBROIDS	UTER FIBROID ENLARGE
					-	-	106	PRE-CANCER CELLS IN UTERUS	CARCINOMA ENDOMETR
					-	-	117	VAGINAL BLEEDING	HEM VAGINAL
			69	Male	-	-	12	PROSTATIC HYPERTROPHY	PROSTAT DIS
			74	Female	-	-	-	URINARY FREQUENCY	URIN FREQUENCY
					-	-	272	URINARY URGENCY	URIN URGENCY
	M27300019				-	-	-	UTERINE DESCENSUS	UTER DIS
			47	Male	+	-	-	BLADDER CARCINOMA	CARCINOMA BLADDER
					0	-	77	PAPILLARY BLADDER CARCINOMA	CARCINOMA BLADDER

Note: mglvl = '+' indicates onset date missing; '<' onset prior to date of first dose; '>' onset after date of last dose; '-' dose level not available

Appendix 4.13.1.1.1
 % and 95% C.I. of Patients with Adverse Events (TES Reported in >= 1% of the Patients in the Pramipexole Group)
 Group: All Double-Blind Placebo Controlled Studies for Early Parkinson's Disease (Early Controlled Studies: 1, 4, & 21)

Body System	Number (%) of Patients						t difference	95% C.I. for t difference
	Pramipexole			Placebo				
	n	t	95% C.I.	n	t	95% C.I.		
Total Patients (N)	388			235				
All Body Systems	344	88.7	(85.0, 91.6)	202	86.0	(80.7, 90.0)	2.7	(-3.1, 8.5)
BODY AS A WHOLE	205	52.8	(47.7, 57.8)	150	63.8	(57.3, 69.9)	-11.0	(-19.2, -2.8)
...INFECT	59	15.2	(11.9, 19.3)	52	22.1	(17.1, 28.1)	-6.9	(-13.6, -0.2)
...HEADACHE	55	14.2	(11.0, 18.2)	37	15.7	(11.4, 21.1)	-1.5	(-7.6, 4.6)
...ASTHENIA	54	13.9	(10.7, 17.8)	27	11.5	(7.8, 16.5)	2.4	(-3.3, 8.1)
...PAIN	51	13.1	(10.0, 17.0)	45	19.1	(14.4, 24.8)	-6.0	(-12.4, 0.4)
...INJURY ACCID	34	8.8	(6.3, 12.2)	20	8.5	(5.4, 13.0)	0.3	(-4.6, 5.2)
...PAIN BACK	31	8.0	(5.6, 11.3)	20	8.5	(5.4, 13.0)	-0.5	(-5.3, 4.3)
...PAIN ABDO	20	5.2	(3.3, 8.0)	15	6.4	(3.8, 10.5)	-1.2	(-5.4, 3.0)
...EDEMA GENERAL	19	4.9	(3.1, 7.7)	7	3.0	(1.3, 6.3)	1.9	(-1.5, 5.3)
...FLU SYND	10	2.6	(1.3, 4.9)	6	2.6	(1.1, 5.8)	0.0	(-2.9, 2.9)
...MALAISE	7	1.8	(0.8, 3.8)	2	0.9	(0.2, 3.4)	0.9	(-1.2, 3.0)
...ALLERG REACT	6	1.5	(0.6, 3.4)	4	1.7	(0.5, 4.6)	-0.2	(-2.6, 2.2)
...REACT UNEVAL	6	1.5	(0.6, 3.4)	2	0.9	(0.2, 3.4)	0.6	(-1.5, 2.7)
...PAIN CHEST	5	1.3	(0.5, 3.2)	11	4.7	(2.5, 8.5)	-3.4	(-6.7, -0.1)
...PAIN NECK	5	1.3	(0.5, 3.2)	5	2.1	(0.8, 5.1)	-0.8	(-3.3, 1.7)
...FEVER	4	1.0	(0.3, 2.8)	1	0.4	(0.0, 2.7)	0.6	(-1.0, 2.2)
CARDIOVASCULAR SYSTEM	50	12.9	(9.8, 16.7)	38	16.2	(11.9, 21.7)	-3.3	(-9.4, 2.8)
...HYPOTENS POST	30	7.7	(5.3, 10.9)	21	8.9	(5.7, 13.5)	-1.2	(-6.0, 3.6)
...VASODILAT	11	2.8	(1.5, 5.1)	10	4.3	(2.2, 8.0)	-1.5	(-4.9, 1.9)

(CONTINUED)
 n = Number of patients reporting an adverse event during treatment
 N = Intent-to-treat population
 Note: Difference refers to p(Pramipexole) - p(Placebo) .

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Body System	Number (t) of Patients							t difference	95% C.I. for t difference
	Pramipexole			Placebo					
	n	t	95% C.I.	n	t	95% C.I.			
...HYPERTENS	6	1.5	(0.6, 3.4)	4	1.7	(0.5, 4.6)	-0.2	(-2.6, 2.2)	
...SYNCOPE	5	1.3	(0.5, 3.2)	2	0.9	(0.2, 3.4)	0.4	(-1.6, 2.4)	
...TACHYCARDIA	5	1.3	(0.5, 3.2)	3	1.3	(0.3, 4.0)	0.0	(-2.2, 2.2)	
DIGESTIVE SYSTEM	181	46.6	(41.6, 51.7)	94	40.0	(33.7, 46.6)	6.6	(-1.7, 14.9)	
...NAUSEA	107	27.6	(23.3, 32.4)	42	17.9	(13.3, 23.5)	9.7	(2.7, 16.7)	
...CONSTIP	53	13.7	(10.5, 17.6)	14	6.0	(3.5, 10.1)	7.7	(2.8, 12.6)	
...DYSPEPSIA	28	7.2	(4.9, 10.4)	16	6.8	(4.1, 11.0)	0.4	(-4.1, 4.9)	
...ANOREXIA	17	4.4	(2.7, 7.1)	5	2.1	(0.8, 5.1)	2.3	(-0.8, 5.4)	
...DIARRHEA	17	4.4	(2.7, 7.1)	18	7.7	(4.8, 12.1)	-3.3	(-7.6, 1.0)	
...DRY MOUTH	13	3.4	(1.9, 5.9)	16	6.8	(4.1, 11.0)	-3.4	(-7.4, 0.6)	
...SALIVA INC	10	2.6	(1.3, 4.9)	7	3.0	(1.3, 6.3)	-0.4	(-3.4, 2.6)	
...DYSPHAGIA	7	1.8	(0.8, 3.8)	1	0.4	(0.0, 2.7)	1.4	(-0.5, 3.3)	
...FLATUL	7	1.8	(0.8, 3.8)	4	1.7	(0.5, 4.6)	0.1	(-2.4, 2.6)	
...TOOTH DIS	7	1.8	(0.8, 3.8)	4	1.7	(0.5, 4.6)	0.1	(-2.4, 2.6)	
...VOMIT	7	1.8	(0.8, 3.8)	8	3.4	(1.6, 6.8)	-1.6	(-4.6, 1.4)	
METABOLIC & NUTRITIONAL SYSTEM	31	8.0	(5.6, 11.3)	14	6.0	(3.5, 10.1)	2.0	(-2.4, 6.4)	
...EDEMA PERIPH	19	4.9	(3.1, 7.7)	10	4.3	(2.2, 8.0)	0.6	(-3.1, 4.3)	
...WEIGHT DEC	7	1.8	(0.8, 3.8)	1	0.4	(0.0, 2.7)	1.4	(-0.5, 3.3)	
...CREATINE PK INC	5	1.3	(0.5, 3.2)	3	1.3	(0.3, 4.0)	0.0	(-2.2, 2.2)	
MUSCULO SKELETAL SYSTEM	22	5.7	(3.7, 8.6)	12	5.1	(2.8, 9.0)	0.6	(-3.4, 4.6)	
...CRAMPS LEG	17	4.4	(2.7, 7.1)	9	3.8	(1.9, 7.3)	0.6	(-2.9, 4.1)	

(CONTINUED)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

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Body System	Number (%) of Patients							t difference	95% C.I. for t difference
	Pramipexole			Placebo					
	n	t	95% C.I.	n	t	95% C.I.			
...TWITCH	6	1.5	(0.6, 3.4)	3	1.3	(0.3, 4.0)	0.2	(-2.0, 2.4)	
NERVOUS SYSTEM	258	66.5	(61.5, 71.1)	138	58.7	(52.1, 65.0)	7.8	(-0.4, 16.0)	
...DIZZINESS	97	25.0	(20.8, 29.7)	57	24.3	(19.1, 30.4)	0.7	(-6.6, 8.0)	
...SOMNOLENCE	85	21.9	(18.0, 26.4)	21	8.9	(5.7, 13.5)	13.0	(7.2, 18.8)	
...INSOMNIA	66	17.0	(13.5, 21.2)	27	11.5	(7.8, 16.5)	5.5	(-0.4, 11.4)	
...TREMOR	37	9.5	(6.9, 13.0)	39	16.6	(12.2, 22.1)	-7.1	(-13.0, -1.2)	
...HALLUCIN	35	9.0	(6.4, 12.4)	6	2.6	(1.1, 5.8)	6.4	(2.6, 10.2)	
...HYPERTONIA	23	5.9	(3.9, 8.9)	18	7.7	(4.8, 12.1)	-1.8	(-6.3, 2.7)	
...DEPRESSION	22	5.7	(3.7, 8.6)	17	7.2	(4.4, 11.5)	-1.5	(-5.9, 2.9)	
...ANXIETY	18	4.6	(2.8, 7.3)	11	4.7	(2.5, 8.5)	-0.1	(-3.9, 3.7)	
...DREAM ABNORM	17	4.4	(2.7, 7.1)	10	4.3	(2.2, 8.0)	0.1	(-3.5, 3.7)	
...CONFUS	16	4.1	(2.4, 6.7)	3	1.3	(0.3, 4.0)	2.8	(0.0, 5.6)	
...AMNESIA	14	3.6	(2.1, 6.1)	4	1.7	(0.5, 4.6)	1.9	(-0.9, 4.7)	
...ATAXIA	13	3.4	(1.9, 5.9)	19	8.1	(5.1, 12.5)	-4.7	(-9.0, -0.4)	
...EXTRAPYR SYND	13	3.4	(1.9, 5.9)	24	10.2	(6.8, 15.0)	-6.8	(-11.4, -2.2)	
...HYPESTHESIA	11	2.8	(1.5, 5.1)	2	0.9	(0.2, 3.4)	1.9	(-0.5, 4.3)	
...GAIT ABNORM	8	2.1	(1.0, 4.2)	6	2.6	(1.1, 5.8)	-0.5	(-3.3, 2.3)	
...DYSTONIA	7	1.8	(0.8, 3.8)	3	1.3	(0.3, 4.0)	0.5	(-1.8, 2.8)	
...AKATHISIA	6	1.5	(0.6, 3.4)	0	0.0	(0.0, 2.0)	1.5	(-0.1, 3.1)	
...HYPOKINESIA	6	1.5	(0.6, 3.4)	12	5.1	(2.8, 9.0)	-3.6	(-7.0, -0.2)	
...THINKING ABNORM	6	1.5	(0.6, 3.4)	1	0.4	(0.0, 2.7)	1.1	(-0.7, 2.9)	

(CONTINUED)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Prämiopexole) - p(Placebo).

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	Number (%) of Patients							t difference	95% C.I. for t difference
	Pramipexole			Placebo					
	n	t	95% C.I.	n	t	95% C.I.			
Body System									
...LIBIDO DEC	5	1.3	(0.5, 3.2)	0	0.0	(0.0, 2.0)	1.3		(-0.2, 2.8)
...MYOCLONUS	5	1.3	(0.5, 3.2)	1	0.4	(0.0, 2.7)	0.9		(-0.8, 2.6)
...NERVOUSNESS	5	1.3	(0.5, 3.2)	5	2.1	(0.8, 5.1)	-0.8		(-3.3, 1.7)
...PARESTHESIA	5	1.3	(0.5, 3.2)	7	3.0	(1.3, 6.3)	-1.7		(-4.5, 1.1)
...VERTIGO	5	1.3	(0.5, 3.2)	13	5.5	(3.1, 9.5)	-4.2		(-7.7, -0.7)
...PARALYSIS	4	1.0	(0.3, 2.8)	4	1.7	(0.5, 4.6)	-0.7		(-3.0, 1.6)
RESPIRATORY SYSTEM	48	12.4	(9.4, 16.2)	37	15.7	(11.4, 21.1)	-3.3		(-9.3, 2.7)
...PHARYNGITIS	13	3.4	(1.9, 5.9)	8	3.4	(1.6, 6.8)	0.0		(-3.3, 3.3)
...SINUSITIS	13	3.4	(1.9, 5.9)	9	3.8	(1.9, 7.3)	-0.4		(-3.8, 3.0)
...RHINITIS	12	3.1	(1.7, 5.5)	8	3.4	(1.6, 6.8)	-0.3		(-3.5, 2.9)
...DYSPNEA	9	2.3	(1.1, 4.5)	6	2.6	(1.1, 5.8)	-0.3		(-3.2, 2.6)
...COUGH INC	8	2.1	(1.0, 4.2)	7	3.0	(1.3, 6.3)	-0.9		(-3.8, 2.0)
...VOICE ALTERAT	5	1.3	(0.5, 3.2)	7	3.0	(1.3, 6.3)	-1.7		(-4.5, 1.1)
SKIN & APPENDAGES	30	7.7	(5.3, 10.9)	27	11.5	(7.8, 16.5)	-3.8		(-9.0, 1.4)
...RASH	15	3.9	(2.3, 6.5)	12	5.1	(2.8, 9.0)	-1.2		(-5.0, 2.6)
...SWEAT	13	3.4	(1.9, 5.9)	14	6.0	(3.5, 10.1)	-2.6		(-6.5, 1.3)
...PRURITUS	5	1.3	(0.5, 3.2)	2	0.9	(0.2, 3.4)	0.4		(-1.6, 2.4)
SPECIAL SENSES	37	9.5	(6.9, 13.0)	14	6.0	(3.5, 10.1)	3.5		(-1.1, 8.1)
...ACCOMMODATION ABNORM	11	2.8	(1.5, 5.1)	6	2.6	(1.1, 5.8)	0.2		(-2.8, 3.2)
...VISION ABNORM	10	2.6	(1.3, 4.9)	0	0.0	(0.0, 2.0)	2.6		(0.7, 4.5)
...TINNITUS	5	1.3	(0.5, 3.2)	2	0.9	(0.2, 3.4)	0.4		(-1.6, 2.4)

(CONTINUED)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

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Body System	Number (%) of Patients							% difference	95% C.I. for % difference
	Pramipexole			Placebo					
	n	%	95% C.I.	n	%	95% C.I.			
...CONJUNCTIVITIS	4	1.0	(0.3, 2.8)	3	1.3	(0.3, 4.0)	-0.3	(-2.4, 1.8)	
...DIPLOPIA	4	1.0	(0.3, 2.8)	2	0.9	(0.2, 3.4)	0.1	(-1.8, 2.0)	
...TASTE PERVERS	4	1.0	(0.3, 2.8)	2	0.9	(0.2, 3.4)	0.1	(-1.8, 2.0)	
UROGENITAL SYSTEM	24	6.2	(4.1, 9.2)	24	10.2	(6.8, 15.0)	-4.0	(-8.9, 0.9)	
...INFECT URIN TRACT	11	2.8	(1.5, 5.1)	12	5.1	(2.8, 9.0)	-2.3	(-5.9, 1.3)	
...URIN FREQUENCY	8	2.1	(1.0, 4.2)	10	4.3	(2.2, 8.0)	-2.2	(-5.5, 1.1)	
...IMPOTENCE	7	1.8	(0.8, 3.8)	3	1.3	(0.3, 4.0)	0.5	(-1.8, 2.8)	

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n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

Appendix 4.13.1.2.1
 % and 95% C.I. of Patients with Adverse Events (TES Reported in >= 1% of the Patients in the Pramipexole Group)
 Group: All Double-Blind Placebo Controlled Studies for Advanced Parkinson's Disease (Advanced Controlled Studies: 10, 19, 20 & 22)

Body System	Number (%) of Patients							t difference	95% C.I. for t difference
	Pramipexole			Placebo					
	n	t	95% C.I.	n	t	95% C.I.			
Total Patients (N)	260			264					
All Body Systems	245	94.2	(90.4, 96.6)	237	89.8	(85.3, 93.1)	4.4	(-0.6, 9.4)	
BODY AS A WHOLE	137	52.7	(46.4, 58.9)	133	50.4	(44.2, 56.6)	2.3	(-6.6, 11.2)	
...INJURY ACCID	43	16.5	(12.3, 21.7)	39	14.8	(10.9, 19.8)	1.7	(-4.9, 8.3)	
...PAIN	31	11.9	(8.3, 16.6)	43	16.3	(12.2, 21.4)	-4.4	(-10.7, 1.9)	
...ASTHENIA	26	10.0	(6.8, 14.5)	21	8.0	(5.1, 12.1)	2.0	(-3.3, 7.3)	
...INFECT	26	10.0	(6.8, 14.5)	36	13.6	(9.8, 18.5)	-3.6	(-9.5, 2.3)	
...HEADACHE	23	8.8	(5.8, 13.1)	38	14.4	(10.5, 19.4)	-5.6	(-11.4, 0.2)	
...PAIN BACK	14	5.4	(3.1, 9.1)	18	6.8	(4.2, 10.7)	-1.4	(-5.9, 3.1)	
...FLU SYND	12	4.6	(2.5, 8.1)	18	6.8	(4.2, 10.7)	-2.2	(-6.5, 2.1)	
...EDEMA GENERAL	10	3.8	(1.9, 7.1)	7	2.7	(1.2, 5.7)	1.1	(-2.3, 4.5)	
...PAIN ABDO	10	3.8	(1.9, 7.1)	10	3.8	(1.9, 7.1)	0.0	(-3.7, 3.7)	
...PAIN CHEST	8	3.1	(1.5, 6.2)	4	1.5	(0.5, 4.1)	1.6	(-1.3, 4.5)	
...MALAISE	7	2.7	(1.2, 5.7)	5	1.9	(0.7, 4.6)	0.8	(-2.1, 3.7)	
...PAIN NECK	4	1.5	(0.5, 4.1)	4	1.5	(0.5, 4.1)	0.0	(-2.5, 2.5)	
CARDIOVASCULAR SYSTEM	148	56.9	(50.6, 63.0)	144	54.5	(48.3, 60.6)	2.4	(-6.5, 11.3)	
...HYPOTENS POST	137	52.7	(46.4, 58.9)	127	48.1	(42.0, 54.3)	4.6	(-4.3, 13.5)	
...HYPERTENS	7	2.7	(1.2, 5.7)	7	2.7	(1.2, 5.7)	0.0	(-3.2, 3.2)	
...HYPOTENS	6	2.3	(0.9, 5.2)	8	3.0	(1.4, 6.1)	-0.7	(-3.8, 2.4)	
...VASODILAT	5	1.9	(0.7, 4.7)	7	2.7	(1.2, 5.7)	-0.8	(-3.7, 2.1)	
...SYNCOPE	4	1.5	(0.5, 4.1)	7	2.7	(1.2, 5.7)	-1.2	(-4.0, 1.6)	

(CONTINUED)
 n = Number of patients reporting an adverse event during treatment
 N = Intent-to-treat population
 Note: Difference refers to p(Pramipexole) - p(Placebo) .

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Body System	Number (%) of Patients							t difference	95% C.I. for % difference
	Pramipexole			Placebo					
	n	%	95% C.I.	n	%	95% C.I.			
...PALPITAT	3	1.2	(0.3, 3.7)	4	1.5	(0.5, 4.1)	-0.3	(-2.7, 2.1)	
DIGESTIVE SYSTEM	110	42.3	(36.3, 48.6)	110	41.7	(35.7, 47.9)	0.6	(-8.2, 9.4)	
...NAUSEA	58	22.3	(17.5, 27.9)	61	23.1	(18.3, 28.7)	-0.8	(-8.4, 6.8)	
...CONSTIP	26	10.0	(6.8, 14.5)	23	8.7	(5.7, 12.9)	1.3	(-4.1, 6.7)	
...DRY MOUTH	17	6.5	(3.9, 10.4)	7	2.7	(1.2, 5.7)	3.8	(-0.2, 7.8)	
...ANOREXIA	14	5.4	(3.1, 9.1)	18	6.8	(4.2, 10.7)	-1.4	(-5.9, 3.1)	
...DYSPEPSIA	13	5.0	(2.8, 8.6)	17	6.4	(3.9, 10.2)	-1.4	(-5.7, 2.9)	
...DIARRHEA	10	3.8	(1.9, 7.1)	11	4.2	(2.2, 7.6)	-0.4	(-4.1, 3.3)	
...SALIVA INC	7	2.7	(1.2, 5.7)	11	4.2	(2.2, 7.6)	-1.5	(-5.0, 2.0)	
...TOOTH DIS	7	2.7	(1.2, 5.7)	8	3.0	(1.4, 6.1)	-0.3	(-3.5, 2.9)	
...VOMIT	5	1.9	(0.7, 4.7)	12	4.5	(2.4, 8.0)	-2.6	(-6.0, 0.8)	
...DYSPHAGIA	3	1.2	(0.3, 3.7)	5	1.9	(0.7, 4.6)	-0.7	(-3.2, 1.8)	
...FLATUL	3	1.2	(0.3, 3.7)	2	0.8	(0.1, 3.1)	0.4	(-1.7, 2.5)	
METABOLIC & NUTRITIONAL SYSTEM	9	3.5	(1.7, 6.7)	3	1.1	(0.3, 3.5)	2.4	(-0.5, 5.3)	
...EDEMA PERIPH	6	2.3	(0.9, 5.2)	2	0.8	(0.1, 3.1)	1.5	(-1.0, 4.0)	
...CREATINE PK INC	3	1.2	(0.3, 3.7)	1	0.4	(0.0, 2.5)	0.8	(-1.1, 2.7)	
MUSCULO SKELETAL SYSTEM	43	16.5	(12.3, 21.7)	28	10.6	(7.3, 15.1)	5.9	(-0.3, 12.1)	
...CRAMPS LEG	14	5.4	(3.1, 9.1)	12	4.5	(2.4, 8.0)	0.9	(-3.2, 5.0)	
...MYALGIA	10	3.8	(1.9, 7.1)	13	4.9	(2.7, 8.4)	-1.1	(-5.0, 2.8)	
...ARTHRITIS	7	2.7	(1.2, 5.7)	3	1.1	(0.3, 3.5)	1.6	(-1.1, 4.3)	
...TWITCH	6	2.3	(0.9, 5.2)	0	0.0	(0.0, 1.8)	2.3	(0.1, 4.5)	

(CONTINUED)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

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Body System	Number (%) of Patients								t difference	95% C.I. for t difference
	Pramipexole				Placebo					
	n	t	95% C.I.	n	t	95% C.I.				
...BURSITIS	4	1.5	(0.5, 4.1)	1	0.4	(0.0, 2.5)	1.1	(-0.9, 3.1)		
...ARTHRALGIA	3	1.2	(0.3, 3.7)	5	1.9	(0.7, 4.6)	-0.7	(-3.2, 1.8)		
...MYASTHENIA	3	1.2	(0.3, 3.7)	0	0.0	(0.0, 1.8)	1.2	(-0.5, 2.9)		
NERVOUS SYSTEM	213	81.9	(76.6, 86.3)	199	75.4	(69.7, 80.4)	6.5	(-0.9, 13.9)		
...DYSKINESIA	123	47.3	(41.1, 53.6)	83	31.4	(25.9, 37.4)	15.9	(7.3, 24.5)		
...EXTRAPYR SYND	72	27.7	(22.4, 33.6)	68	25.8	(20.7, 31.6)	1.9	(-6.1, 9.9)		
...INSOMNIA	70	26.9	(21.7, 32.8)	57	21.6	(16.9, 27.2)	5.3	(-2.4, 13.0)		
...DIZZINESS	67	25.8	(20.7, 31.6)	66	25.0	(20.0, 30.8)	0.8	(-7.0, 8.6)		
...HALLUCIN	43	16.5	(12.3, 21.7)	10	3.8	(1.9, 7.1)	12.7	(7.3, 18.1)		
...DREAM ABNORM	28	10.8	(7.4, 15.4)	25	9.5	(6.4, 13.9)	1.3	(-4.3, 6.9)		
...CONFUS	26	10.0	(6.8, 14.5)	19	7.2	(4.5, 11.2)	2.8	(-2.4, 8.0)		
...SOMNOLENCE	23	8.8	(5.8, 13.1)	16	6.1	(3.6, 9.9)	2.7	(-2.2, 7.6)		
...DEPRESSION	22	8.5	(5.5, 12.7)	44	16.7	(12.5, 21.9)	-8.2	(-14.2, -2.2)		
...DYSTONIA	21	8.1	(5.2, 12.3)	19	7.2	(4.5, 11.2)	0.9	(-4.0, 5.8)		
...TREMOR	19	7.3	(4.6, 11.3)	38	14.4	(10.5, 19.4)	-7.1	(-12.8, -1.4)		
...GAIT ABNORM	18	6.9	(4.3, 10.9)	13	4.9	(2.7, 8.4)	2.0	(-2.4, 6.4)		
...HYPERTONIA	17	6.5	(3.9, 10.4)	16	6.1	(3.6, 9.9)	0.4	(-4.1, 4.9)		
...AMNESIA	15	5.8	(3.4, 9.6)	11	4.2	(2.2, 7.6)	1.6	(-2.5, 5.7)		
...HYPOKINESIA	15	5.8	(3.4, 9.6)	22	8.3	(5.4, 12.5)	-2.5	(-7.3, 2.3)		
...ATAXIA	12	4.6	(2.5, 8.1)	13	4.9	(2.7, 8.4)	-0.3	(-4.3, 3.7)		
...ANXIETY	9	3.5	(1.7, 6.7)	12	4.5	(2.4, 8.0)	-1.0	(-4.7, 2.7)		

(CONTINUED)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

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	Number (†) of Patients								† difference	95% C.I. for † difference
	Pramipexole				Placebo					
	n	†	95% C.I.	n	†	95% C.I.				
Body System										
...PARESTHESIA	8	3.1	(1.5, 6.2)	9	3.4	(1.7, 6.6)		-0.3	(-3.7, 3.1)	
...AKATHISIA	7	2.7	(1.2, 5.7)	6	2.3	(0.9, 5.2)		0.4	(-2.7, 3.5)	
...THINKING ABNORM	7	2.7	(1.2, 5.7)	4	1.5	(0.5, 4.1)		1.2	(-1.6, 4.0)	
...APATHY	6	2.3	(0.9, 5.2)	12	4.5	(2.4, 8.0)		-2.2	(-5.7, 1.3)	
...HYPESTHESIA	5	1.9	(0.7, 4.7)	4	1.5	(0.5, 4.1)		0.4	(-2.2, 3.0)	
...PARANOID REACT	5	1.9	(0.7, 4.7)	1	0.4	(0.0, 2.5)		1.5	(-0.7, 3.7)	
...NERVOUSNESS	4	1.5	(0.5, 4.1)	7	2.7	(1.2, 5.7)		-1.2	(-4.0, 1.6)	
...DELUSIONS	3	1.2	(0.3, 3.7)	1	0.4	(0.0, 2.5)		0.8	(-1.1, 2.7)	
...SLEEP DIS	3	1.2	(0.3, 3.7)	0	0.0	(0.0, 1.8)		1.2	(-0.5, 2.9)	
...VERTIGO	3	1.2	(0.3, 3.7)	4	1.5	(0.5, 4.1)		-0.3	(-2.7, 2.1)	
RESPIRATORY SYSTEM	29	11.2	(7.8, 15.8)	19	7.2	(4.5, 11.2)		4.0	(-1.3, 9.3)	
...DYSPNEA	10	3.8	(1.9, 7.1)	8	3.0	(1.4, 6.1)		0.8	(-2.7, 4.3)	
...RHINITIS	7	2.7	(1.2, 5.7)	3	1.1	(0.3, 3.5)		1.6	(-1.1, 4.3)	
...SINUSITIS	6	2.3	(0.9, 5.2)	4	1.5	(0.5, 4.1)		0.8	(-1.9, 3.5)	
...PNEUMONIA	5	1.9	(0.7, 4.7)	0	0.0	(0.0, 1.8)		1.9	(-0.1, 3.9)	
...COUGH INC	4	1.5	(0.5, 4.1)	4	1.5	(0.5, 4.1)		0.0	(-2.5, 2.5)	
...PHARYNGITIS	3	1.2	(0.3, 3.7)	5	1.9	(0.7, 4.6)		-0.7	(-3.2, 1.8)	
SKIN & APPENDAGES	24	9.2	(6.1, 13.6)	22	8.3	(5.4, 12.5)		0.9	(-4.3, 6.1)	
...RASH	9	3.5	(1.7, 6.7)	10	3.8	(1.9, 7.1)		-0.3	(-3.9, 3.3)	
...SWEAT	9	3.5	(1.7, 6.7)	9	3.4	(1.7, 6.6)		0.1	(-3.4, 3.6)	
...SKIN DIS	5	1.9	(0.7, 4.7)	3	1.1	(0.3, 3.5)		0.8	(-1.7, 3.3)	

(CONTINUED)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

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Body System	Number (%) of Patients						t difference	95% C.I. for t difference
	Pramipexole			Placebo				
	n	t	95% C.I.	n	t	95% C.I.		
...PRURITUS	3	1.2	(0.3, 3.7)	2	0.8	(0.1, 3.1)	0.4	(-1.7, 2.5)
SPECIAL SENSES	24	9.2	(6.1, 13.6)	12	4.5	(2.4, 8.0)	4.7	(0.0, 9.4)
...ACCOMMODATION ABNORM	10	3.8	(1.9, 7.1)	6	2.3	(0.9, 5.2)	1.5	(-1.8, 4.8)
...VISION ABNORM	8	3.1	(1.5, 6.2)	2	0.8	(0.1, 3.1)	2.3	(-0.4, 5.0)
...CONJUNCTIVITIS	3	1.2	(0.3, 3.7)	3	1.1	(0.3, 3.5)	0.1	(-2.1, 2.3)
...DIPLOPIA	3	1.2	(0.3, 3.7)	0	0.0	(0.0, 1.8)	1.2	(-0.5, 2.9)
...LACRIMATION DIS	3	1.2	(0.3, 3.7)	2	0.8	(0.1, 3.1)	0.4	(-1.7, 2.5)
UROGENITAL SYSTEM	25	9.6	(6.4, 14.0)	17	6.4	(3.9, 10.2)	3.2	(-1.8, 8.2)
...URIN FREQUENCY	15	5.8	(3.4, 9.6)	7	2.7	(1.2, 5.7)	3.1	(-0.7, 6.9)
...INFECT URIN TRACT	10	3.8	(1.9, 7.1)	9	3.4	(1.7, 6.6)	0.4	(-3.2, 4.0)
...INCONTIN URIN	5	1.9	(0.7, 4.7)	3	1.1	(0.3, 3.5)	0.8	(-1.7, 3.3)

n = Number of patients reporting an adverse event during treatment
N = Intent-to-treat population
Note: Difference refers to p(Pramipexole) - p(Placebo).

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Appendix 4.13.2.1.1
ET Patients In Completed Adequate And Well-Controlled Studies:
Adverse Events Occurring With Frequency Greater Than Or Equal to 10%
By Study Phase Where Event Was First Reported
Date Produced: 10/30/96

Body System	Costart	Pramipexole				Placebo			
		Ascend N(%)	Maint N(%)	Taper N(%)	Total N(%)	Ascend N(%)	Maint N(%)	Taper N(%)	Total N(%)
Total Patients		377(100.00)	346(100.00)	332(100.00)	377(100.00)	222(100.00)	212(100.00)	200(100.00)	222(100.00)
BODY AS A WHOLE	ASTHENIA	36(9.55)	11(3.18)	6(1.81)	53(14.06)	16(7.21)	7(3.30)	4(2.00)	27(12.16)
	HEADACHE	43(11.41)	9(2.60)	1(0.30)	53(14.06)	24(10.81)	12(5.66)		36(16.22)
	INFECT	20(5.31)	34(9.83)	4(1.20)	58(15.38)	20(9.01)	27(12.74)	3(1.50)	50(22.52)
	PAIN	21(5.57)	27(7.80)	3(0.90)	51(13.53)	25(11.26)	18(8.49)	2(1.00)	45(20.27)
	CONSTIP	42(11.14)	9(2.60)	2(0.60)	53(14.06)	8(3.60)	6(2.83)		14(6.31)
DIGESTIVE SYSTEM	NAUSEA	88(23.34)	17(4.91)	1(0.30)	106(28.12)	25(11.26)	15(7.08)	1(0.50)	41(18.47)
	DIZZINESS	69(18.30)	25(7.23)	2(0.60)	96(25.46)	44(19.82)	12(5.66)		56(25.23)
	INSOMNIA	42(11.14)	13(3.76)	10(3.01)	65(17.24)	21(9.46)	6(2.83)		27(12.16)
	SOMNOLENCE	70(18.57)	15(4.34)		85(22.55)	18(8.11)	2(0.94)	1(0.50)	21(9.46)

Includes Studies M/2730/0001 and M/2730/0004

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Appendix 4.13.2.2.1
AT Patients In Completed Adequate And Well-Controlled Studies:
Adverse Events Occurring With Frequency Greater Than Or Equal to 10%
By Study Phase Where Event Was First Reported

Body System	Costart	Pramipexole				Placebo			
		Ascend N(%)	Maint N(%)	Taper N(%)	Total N(%)	Ascend N(%)	Maint N(%)	Taper N(%)	Total N(%)
Total Patients		181(100.00)	169(100.00)	177(100.00)	181(100.00)	178(100.00)	157(100.00)	165(100.00)	178(100.00)
BODY AS A WHOLE	INFECT	8(4.42)	15(8.88)		23(12.71)	12(6.74)	19(12.10)	2(1.21)	33(18.54)
	INJURY ACCID	16(8.84)	24(14.20)	2(1.13)	42(23.20)	17(9.55)	18(11.46)	3(1.82)	39(21.91)
	PAIN	9(4.97)	15(8.88)	1(0.56)	25(13.81)	10(5.62)	20(12.74)	3(1.82)	33(18.54)
CARDIOVASCULAR SYSTEM	HYPOTENS POST	92(50.83)	26(15.38)	5(2.82)	123(67.96)	93(52.25)	16(10.19)	9(5.45)	118(66.29)
DIGESTIVE SYSTEM	CONSTIP	11(6.08)	12(7.10)		23(12.71)	12(6.74)	9(5.73)	1(0.61)	22(12.36)
	NAUSEA	35(19.34)	7(4.14)	2(1.13)	44(24.31)	35(19.66)	13(8.28)	2(1.21)	50(28.09)
NERVOUS SYSTEM	CONFUS	14(7.73)	8(4.73)	1(0.56)	23(12.71)	10(5.62)	6(3.82)	2(1.21)	18(10.11)
	DIZZINESS	43(23.76)	8(4.73)	3(1.69)	54(29.83)	33(18.54)	16(10.19)	2(1.21)	51(28.65)
	DREAM ABNORM	14(7.73)	6(3.55)	1(0.56)	21(11.60)	15(8.43)	5(3.18)		20(11.24)
	DYSKINESIA	99(54.70)	12(7.10)	2(1.13)	113(62.43)	59(33.15)	17(10.83)	1(0.61)	77(43.26)
	EXTRAPYR SYND	12(6.63)	39(23.08)	14(7.91)	65(35.91)	26(14.61)	29(18.47)	6(3.64)	61(34.27)
	HALLUCIN	28(15.47)	6(3.55)	4(2.26)	38(20.99)	6(3.37)	3(1.91)	1(0.61)	10(5.62)
	INSOMNIA	27(14.92)	17(10.06)	7(3.95)	51(28.18)	32(17.98)	16(10.19)	1(0.61)	49(27.53)

Includes Study M/2730/0010

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Appendix 4.13.4.1
Adverse Events By Dose At First Occurrence
ET Patients; Studies 1, 4, & 21

	Dose at First Occurrence									
	0 - 0.75		>0.75 - 1.5		> 1.5 - 3.0		>3.0 - 4.5		>4.5	
	n	%	n	%	n	%	n	%	n	%
Total Patients (N)	387		372		308		234		45	
ASTHENIA	21	5.43	7	1.88	7	2.27	8	3.85	2	4.44
CONSTIP	18	4.65	10	2.69	9	2.92	12	5.13	2	4.44
DIZZINESS	30	7.75	16	4.30	19	6.17	28	11.97	1	2.22
HEADACHE	33	8.53	5	1.34	7	2.27	7	2.99	1	2.22
INFECT	6	1.55	8	2.15	8	2.60	30	12.82	1	2.22
INSOMNIA	21	5.43	15	4.03	8	2.60	11	4.70	0	0.00
NAUSEA	42	10.85	21	5.65	22	7.17	21	8.97	0	0.00
PAIN	11	2.84	4	1.08	9	2.92	21	8.97	3	6.67
SOMNOLENCE	29	7.49	17	4.57	16	5.19	23	9.83	0	0.00

Events with first occurrence during the dose reduction phase have been excluded

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Appendix 4.13.4.2
Adverse Events By Dose At First Occurrence
AT Patients; Studies 10, 19, 20, & 22

	Dose at First Occurrence											
	0 - 0.75			>0.75 - 1.5			>1.5 - 3.0			>3.0 - 4.5		
	n	%		n	%		n	%		n	%	
Total Patients (N)	260			246			226			183		45
DIZZINESS	26	10.00		7	2.85		14	6.19		15	3.54	1
DREAM ABNORM	12	4.62		6	2.44		4	1.77		5	2.73	0
DYSKINESIA	41	15.77		35	14.23		27	11.95		18	9.84	0
EXTRAPYR SYND	5	1.92		5	2.03		11	4.87		30	16.39	0
HALLUCIN	8	3.08		6	2.44		13	5.75		8	4.37	3
HYPOTENS POST	57	21.92		18	7.32		26	11.50		27	14.75	4
INJURY ACCID	8	3.08		5	2.03		10	4.42		18	9.84	0
INSOMNIA	20	7.69		7	2.85		11	4.87		23	12.57	1
NAUSEA	26	10.00		14	5.69		9	3.98		6	3.28	1
PAIN	3	1.15		5	2.03		8	3.54		12	6.56	0
												0.00

Events with first occurrence during the dose reduction phase have been excluded

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Appendix 4.13.6.1
ET Patients Studies 1, 4, & 21
Adverse Events By Age

Age		Costart	Pramipexole (Total Patients = 388)				Placebo (Total Patients = 235)				RR**	Lower 95% CI	Upper 95% CI
			n		Rate		n		Rate				
			n	N*	Rate		n	N*	Rate				
<= 45	ASTHENIA	8	30	0.267		4	23	0.174		1.53	0.53	4.47	
	CONSTIP	3	30	0.100		1	23	0.043		2.30	0.26	20.70	
	DEPRESSION	4	30	0.133		3	23	0.130		1.02	0.25	4.12	
	DIZZINESS	5	30	0.167		5	23	0.217		0.77	0.25	2.34	
	DYSEPSIA	3	30	0.100		1	23	0.043		2.30	0.26	20.70	
	HALLUCIN	3	30	0.100									
	HEADACHE	6	30	0.200		3	23	0.130		1.53	0.43	5.49	
	HYPERTONIA	1	30	0.033		5	23	0.217		0.15	0.02	1.22	
	HYPOTENS POST	3	30	0.100									
	INFECT					9	23	0.391					
	INJURY ACCID	2	30	0.067		2	23	0.087		0.77	0.12	5.04	
	INSOMNIA	10	30	0.333		2	23	0.087		3.83	0.93	15.82	
	NAUSEA	6	30	0.200		5	23	0.217		0.92	0.32	2.64	
	PAIN	6	30	0.200		1	23	0.043		4.60	0.59	35.60	
	PAIN ABDO					2	23	0.087					
	PAIN BACK	1	30	0.033									
	SOMNOLENCE	7	30	0.233		1	23	0.043		5.37	0.71	40.61	
TREMOR	4	30	0.133		4	23	0.174		0.77	0.21	2.74		
45-55	ASTHENIA	8	63	0.127		2	41	0.049		2.60	0.58	11.65	
	CONSTIP	9	63	0.143		3	41	0.073		1.95	0.56	6.79	

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Includes Studies M/27300001, M/27300004, and M/27300021
 * N is the number of patients in each age group
 ** Relative risk computed as rate of PFX / rate of Placebo

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Age	Costart	Pramipexole (Total Patients = 388)			Placebo (Total Patients = 235)			RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate	n	N*	Rate			
45-55	DEPRESSION	4	63	0.063	1	41	0.024	2.60	0.30	22.48
	DIZZINESS	11	63	0.175	7	41	0.171	1.02	0.43	2.42
	DYSPEPSIA	5	63	0.079	1	41	0.024	3.25	0.39	26.86
	HALLUCIN	2	63	0.032	1	41	0.024	1.30	0.12	13.90
	HEADACHE	12	63	0.190	9	41	0.220	0.87	0.40	1.87
	HYPERTONIA	4	63	0.063	3	41	0.073	0.87	0.20	3.68
	HYPOTENS POST	3	63	0.048	2	41	0.049	0.98	0.17	5.53
	INFECT	8	63	0.127	6	41	0.146	0.87	0.32	2.32
	INJURY ACCID	4	63	0.063	2	41	0.049	1.30	0.25	6.73
	INSOMNIA	13	63	0.206	4	41	0.098	2.12	0.74	6.04
	NAUSEA	15	63	0.238	10	41	0.244	0.98	0.49	1.98
	PAIN	8	63	0.127	11	41	0.268	0.47	0.21	1.08
	PAIN ABDO	3	63	0.048	1	41	0.024	1.95	0.21	18.13
	PAIN BACK	4	63	0.063	4	41	0.098	0.65	0.17	2.46
	SOMNOLENCE	10	63	0.159	1	41	0.024	6.51	0.87	48.95
	TREMOR	7	63	0.111	5	41	0.122	0.91	0.31	2.68
	ASTHENIA	19	120	0.158	9	68	0.132	1.20	0.57	2.50
56-65	CONSTIP	16	120	0.133	6	68	0.088	1.51	0.62	3.68
	DEPRESSION	9	120	0.075	7	68	0.103	0.73	0.28	1.87
	DIZZINESS	26	120	0.217	20	68	0.294	0.74	0.45	1.22

(CONTINUED)

Includes Studies M/27300001, M/27300004, and M/27300021
 * N is the number of patients in each age group
 ** Relative risk computed as rate of PTX / rate of Placebo

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Age	Costart	Pramipexole (Total Patients = 388)				Placebo (Total Patients = 235)				RR**	Lower 95% CI	Upper 95% CI
		n		N*		n		N*				
		n	N*	Rate	Rate	n	N*	Rate	Rate			
56-65	DYSPEPSIA	13	120	0.108		4	68	0.059		1.84	0.63	5.43
	HALLUCIN	7	120	0.058		3	68	0.044		1.32	0.35	4.95
	HEADACHE	20	120	0.167		10	68	0.147		1.13	0.56	2.28
	HYPERTONIA	9	120	0.075		6	68	0.088		0.85	0.32	2.23
	HYPOTENS POST	8	120	0.067		9	68	0.132		0.50	0.20	1.24
	INFECT	23	120	0.192		15	68	0.221		0.87	0.49	1.55
	INJURY ACCID	11	120	0.092		6	68	0.088		1.04	0.40	2.68
	INSOMNIA	22	120	0.183		10	68	0.147		1.25	0.63	2.47
	NAUSEA	33	120	0.275		12	68	0.176		1.56	0.86	2.81
	PAIN	12	120	0.100		15	68	0.221		0.45	0.23	0.91
	PAIN ABDO	8	120	0.067		4	68	0.059		1.13	0.35	3.63
	PAIN BACK	14	120	0.117		4	68	0.059		1.98	0.68	5.75
	SOMNOLENCE	24	120	0.200		7	68	0.103		1.94	0.88	4.27
66-75	TREMOR	19	120	0.158		13	68	0.191		0.83	0.44	1.57
	ASTHENIA	11	144	0.076		11	83	0.133		0.58	0.26	1.27
	CONSTIP	21	144	0.146	*	3	83	0.036		4.03	1.24	13.12
	DEPRESSION	4	144	0.028		4	83	0.048		0.58	0.15	2.24
	DIZZINESS	46	144	0.319		19	83	0.229		1.40	0.88	2.21
	DYSPEPSIA	6	144	0.042		8	83	0.096		0.43	0.16	1.21
	HALLUCIN	16	144	0.111		2	83	0.024		4.61	1.09	19.56

(CONTINUED)

Includes Studies M/27300001, M/27300004, and M/27300021
 * N is the number of patients in each age group
 ** Relative risk computed as rate of PPX / rate of Placebo

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Age		Pramipexole (Total Patients = 388)			Placebo (Total Patients = 235)			RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate	n	N*	Rate			
66-75	Cosstart									
	HEADACHE	17	144	0.118	13	83	0.157	0.75	0.39	1.47
	HYPERTONIA	7	144	0.049	3	83	0.036	1.34	0.36	5.06
	HYPOTENS POST	15	144	0.104	9	83	0.108	0.96	0.44	2.10
	INFECT	25	144	0.174	18	83	0.217	0.80	0.47	1.38
	INJURY ACID	14	144	0.097	8	83	0.096	1.01	0.44	2.30
	INSOMNIA	20	144	0.139	9	83	0.108	1.28	0.61	2.65
	NAUSEA	43	144	0.299	12	83	0.145	2.07	1.16	3.63
	PAIN	21	144	0.146	16	83	0.193	0.76	0.42	1.37
	PAIN ABDO	9	144	0.063	5	83	0.060	1.04	0.36	2.99
	PAIN BACK	7	144	0.049	10	83	0.120	0.40	0.16	1.02
	SOMNOLENCE	38	144	0.264	10	83	0.120	2.19	1.15	4.16
	TREMOR	6	144	0.042	15	83	0.181	0.23	0.09	0.57
	ASTHENIA	8	31	0.258	1	20	0.050	5.16	0.70	38.19
	CONSTIP	4	31	0.129	1	20	0.050	2.58	0.31	21.46
> 75	DEPRESSION	1	31	0.032	2	20	0.100	0.32	0.03	3.33
	DIZZINESS	9	31	0.290	6	20	0.300	0.97	0.41	2.30
	DYSPNOEA	1	31	0.032	2	20	0.100	0.32	0.03	3.33
	HALLUCIN	7	31	0.226						
	HEADACHE				2	20	0.100			
	HYPERTONIA	2	31	0.065	1	20	0.050	1.29	0.13	13.31

(CONTINUED)

Includes Studies M/2730/0001, M/2730/0004, and M/2730/0021

* N is the number of patients in each age group

** Relative risk computed as rate of PPX / rate of Placebo

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Pramipexole (Total Patients = 388)											Placebo (Total Patients = 235)			RR**	Lower 95% CI	Upper 95% CI	
n		N*		Rate		n		N*		Rate							
Age	Costart																
> 75	HYPOTENS POST	1	31	0.032	1	20	0.050					†	0.65	0.04	9.74		
	INFECT	3	31	0.097	4	20	0.200						0.48	0.12	1.94		
	INJURY ACCID	3	31	0.097	2	20	0.100						0.97	0.18	5.23		
	INSOMNIA	1	31	0.032	2	20	0.100						0.32	0.03	3.33		
	NAUSEA	10	31	0.323	3	20	0.150						2.15	0.67	6.87		
	PAIN	4	31	0.129	2	20	0.100						1.29	0.26	6.40		
	PAIN ABDO					3	20	0.150									
	PAIN BACK	5	31	0.161	2	20	0.100						1.61	0.35	7.53		
	SOMNOLENCE	6	31	0.194	2	20	0.100						1.94	0.43	8.66		
	TREMOR	1	31	0.032	2	20	0.100						0.32	0.03	3.33		

* N is the number of patients in each age group
 ** Relative risk computed as rate of PPX / rate of Placebo

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Appendix 4.13.6.2
AT Patients Studies 10, 19, 20, & 22
Adverse Events By Age

		Pranipexole (Total Patients = 260)			Placebo (Total Patients = 264)			RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate	n	N*	Rate			
Age	Costart									
	<= 45									
	AMNESIA				1	11	0.091			
	ANOREXIA				2	11	0.182			
	ASTHENIA	1	10	0.100	1	11	0.091	1.10	0.08	15.36
	CONFUS	1	10	0.100						
	CONSTIP	1	10	0.100						
	CRAMPS LEG	1	10	0.100						
	DEPRESSION	2	10	0.200	5	11	0.455	0.44	0.11	1.78
	DIZZINESS	3	10	0.300	3	11	0.273	1.10	0.28	4.25
	DREAM ABNORM	1	10	0.100	2	11	0.182	0.55	0.06	5.18
	DRY MOUTH				1	11	0.091			
	DYSKINESIA	8	10	0.800	5	11	0.455	1.76	0.86	3.61
	DYSPERSIA	1	10	0.100	1	11	0.091	1.10	0.08	15.36
	DYSTONIA				1	11	0.091			
	EXTRAPYR SYND	3	10	0.300	4	11	0.364	0.82	0.24	2.82
	HEADACHE				2	11	0.182			
	HYPERTONIA				1	11	0.091			
	HYPOKINESIA	2	10	0.200	1	11	0.091	2.20	0.23	20.72
	HYPOTENS POST	6	10	0.600	3	11	0.273	2.20	0.74	6.54
	INFECT	2	10	0.200	2	11	0.182	1.10	0.19	6.41
	INJURY ACCID	1	10	0.100	1	11	0.091	1.10	0.08	15.36

(CONTINUED)

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Age		Pramipexole (Total Patients = 260)										Placebo (Total Patients = 264)					RR**	Lower 95% CI	Upper 95% CI
		Costart		n		N*		Rate		n		N*		Rate					
< = 45				2	10	0.200				5	11	0.455			0.44	0.11	1.78		
				3	10	0.300				3	11	0.273			1.10	0.28	4.25		
				2	10	0.200				1	11	0.091			2.20	0.23	20.72		
										1	11	0.091							
				1	10	0.100				1	11	0.091			1.10	0.08	15.36		
				1	10	0.100				2	11	0.182			0.55	0.06	5.18		
				4	48	0.083				4	51	0.078			1.06	0.28	4.01		
				4	48	0.083				2	51	0.039			2.12	0.41	11.08		
				7	48	0.146				2	51	0.039			3.72	0.81	17.02		
				5	48	0.104				3	51	0.059			1.77	0.45	7.01		
				5	48	0.104				1	51	0.020			5.31	0.64	43.84		
				4	48	0.083				3	51	0.059			1.42	0.33	6.00		
				6	48	0.125				6	51	0.118			1.06	0.37	3.07		
				8	48	0.167				10	51	0.196			0.85	0.37	1.97		
				4	48	0.083				3	51	0.059			1.42	0.33	6.00		
				5	48	0.104													
				25	48	0.521				22	51	0.431			1.21	0.80	1.83		
				2	48	0.042				3	51	0.059			0.71	0.12	4.06		
				4	48	0.083				4	51	0.078			1.06	0.28	4.01		
				21	48	0.438				13	51	0.255			1.72	0.97	3.03		

Age		Pramipexole (Total Patients = 260)										Placebo (Total Patients = 264)				RR**	Lower 95% CI	Upper 95% CI
		Costart																
		n	N*	Rate	n	N*	Rate	n	N*	Rate	n	N*	Rate					
45-55	GAIT ABNORM	2	48	0.042			2	51	0.039				1.06	0.16	7.25			
	HALLUCIN	2	48	0.042			1	51	0.020				2.13	0.20	22.68			
	HEADACHE	5	48	0.104			10	51	0.196				0.53	0.20	1.44			
	HYPERTONIA	3	48	0.063			4	51	0.078				0.80	0.19	3.38			
	HYPOKINESIA	5	48	0.104			5	51	0.098				1.06	0.33	3.44			
	HYPOTENS POST	20	48	0.417			23	51	0.451				0.92	0.59	1.45			
	INFECT	5	48	0.104			14	51	0.275				0.38	0.15	0.97			
	INJURY ACCID	5	48	0.104			8	51	0.157				0.66	0.23	1.89			
	INSOMNIA	19	48	0.396			12	51	0.235				1.68	0.92	3.08			
	NAUSEA	11	48	0.229			14	51	0.275				0.83	0.42	1.65			
	PAIN	4	48	0.083			7	51	0.137				0.61	0.19	1.94			
	PAIN BACK	4	48	0.083			6	51	0.118				0.71	0.21	2.36			
	SOMNOLENCE	4	48	0.083			3	51	0.059				1.42	0.33	6.00			
56-65	TREMOR	1	48	0.021			5	51	0.098				0.21	0.03	1.75			
	URIN FREQUENCY	3	48	0.063			2	51	0.039				1.59	0.28	9.13			
	AMNESIA	3	91	0.033			4	90	0.044				0.74	0.17	3.22			
	ANOREXIA	3	91	0.033			8	90	0.089				0.37	0.10	1.35			
	ASTHENIA	12	91	0.132			10	90	0.111				1.19	0.54	2.61			
	CONFUS	3	91	0.033			7	90	0.078				0.42	0.11	1.59			
	CONSTIP	8	91	0.088			10	90	0.111				0.79	0.33	1.91			

(CONTINUED)

APPEARS THIS WAY
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		Pranipexole (Total Patients = 260)				Placebo (Total Patients = 264)				RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate		n	N*	Rate				
Age	Costart											
	56-65	4	91	0.044		6	90	0.067		0.66	0.19	2.26
	CRAMPS LEG	9	91	0.099		17	90	0.189		0.52	0.25	1.11
	DEPRESSION	22	91	0.242		23	90	0.256		0.95	0.57	1.57
	DIZZINESS	12	91	0.132		12	90	0.133		0.99	0.47	2.08
	DREAM ABNORM	6	91	0.066		2	90	0.022		2.97	0.62	14.31
	DRY MOUTH	43	91	0.473		33	90	0.367		1.29	0.91	1.82
	DYSKINESIA	4	91	0.044		8	90	0.089		0.49	0.15	1.58
	DYSPEPSIA	8	91	0.088		8	90	0.089		0.99	0.39	2.52
	DYSTONIA	19	91	0.209		22	90	0.244		0.85	0.50	1.47
	EXTRAPYR SYND	7	91	0.077		5	90	0.056		1.38	0.46	4.20
	GAIT ABNORM	15	91	0.165		4	90	0.044		3.71	1.28	10.75
	HALLUCIN	10	91	0.110		16	90	0.178		0.62	0.30	1.29
	HEADACHE	7	91	0.077		8	90	0.089		0.87	0.33	2.29
	HYPERTONIA	5	91	0.055		8	90	0.089		0.62	0.21	1.82
	HYPOKINESIA	47	91	0.516		45	90	0.500		1.03	0.78	1.38
	HYPOTENS POST	10	91	0.110		7	90	0.078		1.41	0.56	3.55
	INFECT	14	91	0.154		17	90	0.189		0.81	0.43	1.55
	INJURY ACCID	21	91	0.231		25	90	0.278		0.83	0.50	1.37
	INSOMNIA	23	91	0.253		21	90	0.233		1.08	0.65	1.81
	NAUSEA	10	91	0.110		19	90	0.211		0.52	0.26	1.06
	PAIN											

(CONTINUED)

APPEARS THIS WAY
ON ORIGINAL

Age	Costart	Pramipexole (Total Patients = 260)				Placebo (Total Patients = 264)				RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate	n	N*	Rate					
56-65	PAIN BACK	1	91	0.011	6	90	0.067		0.16	0.02	1.34	
	SOMNOLENCE	8	91	0.088	5	90	0.056		1.58	0.54	4.63	
	TREMOR	8	91	0.088	20	90	0.222		0.40	0.18	0.85	
	URIN FREQUENCY	3	91	0.033	3	90	0.033		0.99	0.21	4.77	
66-75	AMNESIA	7	96	0.073	2	98	0.020		3.57	0.76	16.77	
	ANOREXIA	6	96	0.063	2	98	0.020		3.06	0.63	14.80	
	ASTHENIA	5	96	0.052	6	98	0.061		0.85	0.27	2.65	
	CONFUS	13	96	0.135	7	98	0.071		1.90	0.79	4.55	
	CONSTIP	11	96	0.115	10	98	0.102		1.12	0.50	2.52	
	CRAMPS LEG	4	96	0.042	3	98	0.031		1.36	0.31	5.92	
	DEPRESSION	4	96	0.042	14	98	0.143		0.29	0.10	0.85	
	DIZZINESS	28	96	0.292	25	98	0.255		1.14	0.72	1.81	
	DREAM ABNORM	9	96	0.094	8	98	0.082		1.15	0.46	2.85	
	DRY MOUTH	6	96	0.063	4	98	0.041		1.53	0.45	5.26	
	DYSKINESIA	41	96	0.427	19	98	0.194		2.20	1.38	3.51	
	DYSPEPSIA	5	96	0.052	5	98	0.051		1.02	0.31	3.41	
	DYSTONIA	6	96	0.063	5	98	0.051		1.23	0.39	3.88	
	EXTRAPYR SYND	23	96	0.240	23	98	0.235		1.02	0.62	1.69	
	GAIT ABNORM	7	96	0.073	6	98	0.061		1.19	0.42	3.42	
HALLUCIN	22	96	0.229	4	98	0.041		5.61	2.01	15.69		

(CONTINUED)

APPEARS THIS WAY
ON ORIGINAL

Age		Pranipexole (Total Patients = 260)				Placebo (Total Patients = 264)				RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate	n	N*	Rate	n	N*	Rate		
66-75	Costart											
	HEADACHE	7	96	0.073		98	0.092			0.79	0.31	2.05
	HYPERTONIA	6	96	0.063	3	98	0.031			2.04	0.53	7.93
	HYPOKINESIA	3	96	0.031	7	98	0.071			0.44	0.12	1.64
	HYPOTENS POST	52	96	0.542	48	98	0.490			1.11	0.84	1.43
	INFECT	7	96	0.073	12	98	0.122			0.60	0.24	1.43
	INJURY ACCID	17	96	0.177	11	98	0.112			1.58	0.78	3.19
	INSOMNIA	24	96	0.250	13	98	0.133			1.88	1.02	3.48
	NAUSEA	19	96	0.198	20	98	0.204			0.97	0.55	1.70
	PAIN	11	96	0.115	14	98	0.143			0.80	0.38	1.68
	PAIN BACK	6	96	0.063	4	98	0.041			1.53	0.45	5.26
	SOMNOLENCE	10	96	0.104	6	98	0.061			1.70	0.64	4.50
	TREMOR	8	96	0.083	9	98	0.092			0.91	0.37	2.25
	URIN FREQUENCY	9	96	0.094	1	98	0.010			9.19	1.19	71.14
	AMNESIA	1	15	0.067								
	ANOREXIA	1	15	0.067	4	14	0.286			0.23	0.03	1.84
	ASTHENIA	1	15	0.067	2	14	0.143			0.47	0.05	4.60
> 75	CONFUS	4	15	0.267	2	14	0.143			1.87	0.40	8.65
	CONSTIP	1	15	0.067	2	14	0.143			0.47	0.05	4.60
	CRAMPS LEG	1	15	0.067								
	DEPRESSION	1	15	0.067	2	14	0.143			0.47	0.05	4.60

(CONTINUED)

APPEARS THIS WAY
ON ORIGINAL

		Pranipexole (Total Patients = 260)				Placebo (Total Patients = 264)				RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate		n	N*	Rate				
Age	Costart											
	> 75											
	DIZZINESS	6	15	0.400		5	14	0.357		1.12	0.44	2.86
	DREAM ABNORM	2	15	0.133								
	DYSKINESIA	6	15	0.400		4	14	0.286		1.40	0.50	3.94
	DYSPEPSIA	1	15	0.067								
	DYSTONIA	3	15	0.200		1	14	0.071				
	EXTRAPYR SYND	6	15	0.400		6	14	0.429		0.93	0.39	2.22
	GAIT ABNORM	2	15	0.133								
	HALLUCIN	4	15	0.267		1	14	0.071		3.73	0.47	29.45
	HEADACHE	1	15	0.067		1	14	0.071		0.93	0.06	13.54
	HYPERTONIA	1	15	0.067								
	HYPOKINESIA					1	14	0.071				
	HYPOTENS POST	12	15	0.800		8	14	0.571		1.40	0.83	2.35
	INFECT	2	15	0.133		1	14	0.071		1.87	0.19	18.38
	INJURY ACCID	6	15	0.400		2	14	0.143		2.80	0.67	11.64
	INSOMNIA	4	15	0.267		2	14	0.143		1.87	0.40	8.65
	NAUSEA	2	15	0.133		3	14	0.214		0.62	0.12	3.19
	PAIN	4	15	0.267		2	14	0.143		1.87	0.40	8.65
	PAIN BACK	3	15	0.200		1	14	0.071		2.80	0.33	23.87
	SOMNOLENCE					1	14	0.071				
	TREMOR	1	15	0.067		2	14	0.143		0.47	0.05	4.60
	URIN FREQUENCY					1	14	0.071				

* N is the number of patients in each gender

** Relative risk computed as rate of PPX / rate of Placebo

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Appendix 4.13.6.3
ET Patients Studies 1, 4, & 21
Adverse Events By Gender

Sex		Cosiart	Pramipexole (Total Patients = 388)				Placebo (Total Patients = 235)				RR**	Lower 95% CI	Upper 95% CI
			n	N*	Rate	n	N*	Rate					
Male		ASTHENIA	32	251	0.127		10	141	0.071	1.80	0.91	3.55	
		CONSTIP	36	251	0.143		7	141	0.050	2.89	1.32	6.32	
		DEPRESSION	17	251	0.068		5	141	0.035	1.91	0.72	5.07	
		DIZZINESS	57	251	0.227		29	141	0.206	1.10	0.74	1.64	
		DYSPEPSIA	18	251	0.072		11	141	0.078	0.92	0.45	1.89	
		HALLUCIN	24	251	0.096		5	141	0.035	2.70	1.05	6.91	
		HEADACHE	27	251	0.108		16	141	0.113	0.95	0.53	1.70	
		HYPERTONIA	15	251	0.060		10	141	0.071	0.84	0.39	1.83	
		HYPOTENS POST	19	251	0.076		12	141	0.085	0.89	0.44	1.78	
		INFECT	39	251	0.155		33	141	0.234	0.66	0.44	1.01	
		INJURY ACCID	25	251	0.100		9	141	0.064	1.56	0.75	3.25	
		INSOMNIA	45	251	0.179		17	141	0.121	1.49	0.89	2.50	
		NAUSEA	47	251	0.187		16	141	0.113	1.65	0.97	2.80	
		PAIN	29	251	0.116		24	141	0.170	0.68	0.41	1.12	
		PAIN ABDO	12	251	0.048		7	141	0.050	0.96	0.39	2.39	
		PAIN BACK	16	251	0.064		10	141	0.071	0.90	0.42	1.93	
		SOMNOLENCE	60	251	0.239		9	141	0.064	3.75	1.92	7.32	
Female		TREMOR	27	251	0.108		22	141	0.156	0.69	0.41	1.16	
		ASTHENIA	22	137	0.161		17	94	0.181	0.89	0.50	1.58	
		CONSTIP	17	137	0.124		7	94	0.074	1.67	0.72	3.86	

(CONTINUED)

APPEARS THIS WAY
ON ORIGINAL

		Pramipexole (Total Patients = 388)				Placebo (Total Patients = 235)				RR**	Lower 95% CI	Upper 95% CI
Sex		n	N*	Rate	n	N*	Rate	n	N*			
Female	Cosart											
	DEPRESSION	5	137	0.036	12	94	0.128			0.29	0.10	0.78
	DIZZINESS	40	137	0.292	28	94	0.298			0.98	0.65	1.47
	DYSPEPSIA	10	137	0.073	5	94	0.053			1.37	0.48	3.89
	HALLUCIN	11	137	0.080	1	94	0.011			7.55	0.99	57.48
	HEADACHE	28	137	0.204	21	94	0.223			0.91	0.55	1.51
	HYPERTONIA	8	137	0.058	8	94	0.085			0.69	0.27	1.76
	HYPOTENS POST	11	137	0.080	9	94	0.096			0.84	0.36	1.94
	INFECT	20	137	0.146	19	94	0.202			0.72	0.41	1.28
	INJURY ACCID	9	137	0.066	11	94	0.117			0.56	0.24	1.30
	INSOMNIA	21	137	0.153	10	94	0.106			1.44	0.71	2.92
	NAUSEA	60	137	0.438	26	94	0.277			1.58	1.08	2.31
	PAIN	22	137	0.161	21	94	0.223			0.72	0.42	1.23
	PAIN ABDO	8	137	0.058	8	94	0.085			0.69	0.27	1.76
	PAIN BACK	15	137	0.109	10	94	0.106			1.03	0.48	2.19
	SOMNOLENCE	25	137	0.182	12	94	0.128			1.43	0.76	2.70
	TREMOR	10	137	0.073	17	94	0.181			0.40	0.19	0.84

* N is the number of patients in each gender

** Relative risk computed as rate of PPX / rate of Placebo

APPEARS THIS WAY
ON ORIGINAL

Appendix 4.13.6.4
AT Patients Studies 10, 19, 20, & 22
Adverse Events By Gender

Sex		Cosart	Pramipexole (Total Patients = 260)						Placebo (Total Patients = 264)						RR**	Lower 95% CI	Upper 95% CI
			n		N*		Rate		n		N*		Rate				
Male				9	164	0.055		8	173	0.046			1.19	0.47	3.00		
				9	164	0.055		9	173	0.052			1.05	0.43	2.59		
				17	164	0.104		11	173	0.064			1.63	0.79	3.38		
				19	164	0.116		13	173	0.075			1.54	0.79	3.02		
				20	164	0.122		14	173	0.081			1.51	0.79	2.88		
				6	164	0.037		9	173	0.052			0.70	0.26	1.93		
				10	164	0.061		24	173	0.139			0.44	0.22	0.89		
				42	164	0.256		34	173	0.197			1.30	0.87	1.94		
				16	164	0.098		18	173	0.104			0.94	0.50	1.78		
				11	164	0.067		4	173	0.023			2.90	0.94	8.93		
				73	164	0.445		52	173	0.301			1.48	1.11	1.97		
				10	164	0.061		8	173	0.046			1.32	0.53	3.26		
				13	164	0.079		13	173	0.075			1.05	0.50	2.21		
				44	164	0.268		40	173	0.231			1.16	0.80	1.68		
				12	164	0.073		9	173	0.052			1.41	0.61	3.25		
				31	164	0.189		9	173	0.052			3.63	1.79	7.40		
				10	164	0.061		22	173	0.127			0.48	0.23	0.98		
				11	164	0.067		8	173	0.046			1.45	0.60	3.52		
				7	164	0.043		15	173	0.087			0.49	0.21	1.18		
				86	164	0.524		78	173	0.451			1.16	0.93	1.45		

(CONTINUED)

APPEARS THIS WAY
ON ORIGINAL

		Pramipexole (Total Patients = 260)			Placebo (Total Patients = 264)			RR**	Lower 95% CI	Upper 95% CI
		n	N*	Rate	n	N*	Rate			
Sex	Costart									
Male	INFECT	18	164	0.110	25	173	0.145	0.76	0.43	1.34
	INJURY ACCID	29	164	0.177	19	173	0.110	1.61	0.94	2.76
	INSOMNIA	41	164	0.250	35	173	0.202	1.24	0.83	1.84
	NAUSEA	34	164	0.207	34	173	0.197	1.05	0.69	1.61
	PAIN	19	164	0.116	27	173	0.156	0.74	0.43	1.28
	PAIN BACK	10	164	0.061	16	173	0.092	0.66	0.31	1.41
	SOMNOLENCE	17	164	0.104	11	173	0.064	1.63	0.79	3.38
	TREMOR	13	164	0.079	21	173	0.121	0.65	0.34	1.26
	URIN FREQUENCY	8	164	0.049	5	173	0.029	1.69	0.56	5.05
	AMNESIA	6	96	0.063	3	91	0.033	1.90	0.49	7.36
	ANOREXIA	5	96	0.052	9	91	0.099	0.53	0.18	1.51
	ASTHENIA	9	96	0.094	10	91	0.110	0.85	0.36	2.00
	CONFUS	7	96	0.073	6	91	0.066	1.11	0.39	3.17
	CONSTIP	6	96	0.063	9	91	0.099	0.63	0.23	1.70
Female	CRAMPS LEG	8	96	0.083	3	91	0.033	2.53	0.69	9.23
	DEPRESSION	12	96	0.125	20	91	0.220	0.57	0.30	1.10
	DIZZINESS	25	96	0.260	32	91	0.352	0.74	0.48	1.15
	DREAM ABNORM	12	96	0.125	7	91	0.077	1.63	0.67	3.95
	DRY MOUTH	6	96	0.063	3	91	0.033	1.90	0.49	7.36
	DYSKINESIA	50	96	0.521	31	91	0.341	1.53	1.08	2.16

(CONTINUED)

APPEARS THIS WAY
ON ORIGINAL

