Predefined Limits for Laboratory Assays

| Assay | Unit of Measure | Sex | Criterion Value |
|---|---|---|---|
| Hemoglobin | g/dL | M | <10, >18 |
| | | F | <9, >17 |
| Hematocrit | % | M | <30, >54 |
| | | F | <27, >51 |
| RBC | $10^6$/uL | M | <3, >7 |
| | | F | <2.5, >6.5 |
| MCV | fL | | <75, >110 |
| MCH | pg | | <24, >36 |
| MCHC | % | | <30, >38 |
| Platelet Count | cells/$mm^3$ | | <80,000 >600,000 |
| WBC Count | $10^3$/uL | | <3, >13 |
| Neutrophils | % | | <=15 |
| Lymphocytes | % | | <=10, >=80 |
| Monocytes | % | | >=20 |
| Eosinophil | % | | >=10 |
| Basophil | % | | >=10 |
| Bands | % | | >=10 |
| Glucose | mg/dL | | <60, >200 |
| BUN | mg/dL | | >40 |
| Creatinine | mg/dL | | >2.5 |
| Uric Acid | mg/dL | | >10 |
| Total Cholesterol | mg/dL | | >50 |
| Total Bilirubin | mg/dL | | >2.5 |
| Alkaline Phosphatase | U/L | | 2.5 x ULN* |
| LDH | U/L | | 2.5 x ULN |
| SGOT (AST) | U/L | | 2.5 x ULN |
| SGPT (ALT) | U/L | | 2.5 x ULN |
| Creatine Kinase | U/L | | 2.5 x ULN |
| Gamma-Glutamyl Transpeptidase (GGT) | U/L | | 2.5 x ULN |
| Total Protein | g/dL | | <4.5, >9 |
| Calcium | mg/dL | | $\leq$8, $\geq$12 |
| Chloride | mEq/L | | $\leq$90, $\geq$115 |
| Protein Globulin | G/DL | | $\leq$1.0, $\geq$4.0 |

(Continued)

Predefined Limits for Laboratory Assays

| Assay | Unit of Measure | Sex | Criterion Value |
|---|---|---|---|
| Potassium | mEq/L | | ≤3.0, ≥6.0 |
| Sodium | mEq/L | | ≤125, ≥160 |
| Specific Gravity | | | ≤1.005, ≥1.028 |
| pH | | | ≤4.0, ≥9.0 |
| Urine Protein | | | > 1+ |
| Urine Glucose | | | > 1+ |
| Urine Ketone | | | > 2+ |
| Urine RBC | | | > 5 |
| Urine WBC | HPF | M | > 10 |
| | HPF | F | > 20 |
| Urine Casts | | | Present |
| Culture | | | Positive |

* ULN = Upper Limit of Normal Range



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**Summary of All patients With Laboratory Values**
**Exceeding Predefined Limits**
**Group: Adequate and Well-Controlled Studies# for Parkinson's Disease**

| | | Medication | | | | | |
|---|---|---|---|---|---|---|---|
| | | Pramipexole | | | Placebo | | |
| Laboratory Test | | n | N | % | n | N | % |
| Hematology | Hemoglobin | 5 | 547 | 0.91 | 5 | 394 | 1.27 |
| | Hematocrit | 4 | 547 | 0.73 | 5 | 394 | 1.27 |
| | RBC Count | 1 | 547 | 0.18 | 1 | 394 | 0.25 |
| | MCV | 3 | 547 | 0.55 | 2 | 394 | 0.51 |
| | MCH | 5 | 547 | 0.91 | 4 | 394 | 1.02 |
| | MCHC | 4 | 547 | 0.73 | 3 | 394 | 0.76 |
| | WBC Count | 13 | 547 | 2.38 | 15 | 394 | 3.81 |
| | Neutrophils Segs | 0 | 339 | 0 | 0 | 343 | 0 |
| | Bands | 0 | 209 | 0 | 0 | 51 | 0 |
| | Lymphocytes | 16 | 547 | 2.93 | 7 | 394 | 1.78 |
| | Monocytes | 0 | 547 | 0 | 0 | 394 | 0 |
| | Eosinophils | 19 | 547 | 3.47 | 24 | 394 | 6.09 |
| | Basophils | 0 | 547 | 0 | 0 | 394 | 0 |
| | Platelet Count | 3 | 546 | 0.55 | 1 | 394 | 0.25 |
| Blood Chemistry | Glucose | 30 | 547 | 5.48 | 25 | 394 | 6.35 |
| | BUN | 1 | 547 | 0.18 | 2 | 394 | 0.51 |
| | Creatinine | 1 | 547 | 0.18 | 0 | 394 | 0 |
| | Uric Acid | 3 | 547 | 0.55 | 4 | 394 | 1.02 |
| | Cholesterol, Total | 16 | 547 | 2.93 | 14 | 394 | 3.55 |
| | Bilirubin, Total | 0 | 547 | 0 | 1 | 394 | 0.25 |
| | Alkaline Phosphatase | 2 | 547 | 0.37 | 0 | 394 | 0 |
| | LDH | 1 | 547 | 0.18 | 0 | 394 | 0 |
| | SGOT | 4 | 547 | 0.73 | 0 | 394 | 0 |
| | SGPT | 4 | 547 | 0.73 | 2 | 394 | 0.51 |
| | CPK | 19 | 544 | 3.49 | 9 | 392 | 2.30 |
| | GGT | 11 | 547 | 2.01 | 4 | 394 | 1.02 |
| | Protein, Total | 1 | 547 | 0.18 | 0 | 394 | 0 |
| Urinalysis | Urine Protein | 8 | 364 | 2.20 | 2 | 219 | 0.91 |
| | Urine Glucose | 6 | 364 | 1.65 | 5 | 219 | 2.28 |
| | Urine Micro WBC | 12 | 364 | 3.30 | 14 | 219 | 6.39 |
| | Urine Micro RBC | 13 | 364 | 3.57 | 18 | 219 | 8.22 |
| | Urine Ketone | 0 | 364 | 0 | 0 | 219 | 0 |
| | Urine Micro Casts | 6 | 161 | 3.73 | 8 | 169 | 4.73 |
| | Urine Culture | 0 | 0 | 0 | 1 | 1 | 100.00 |

*Source: Appendix C, Table 30.1*
Protocols M/2730/0001, M/2730/0004, and M/2730/0010

| PLACEBO Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments-Relevant Info |
| 0001 | Burch | 46/F/W | -12<br>25<br>53<br>106<br>169<br>232<br>239 | | Angina - 1988; Hypertension; Bypass surgery (for weight control) - 1975; Hypothyroidism - 1968; Prostatism; Osteoarthritis; Back pain; Obesity;<br><br>ECG NSR; Prominent anterior forces; may be artifact | Artane<br>Eldepryl<br>Flagyl<br>Sulfamethoxazole<br>Naproxen<br>Tylenol with codeine<br>Relafen<br>Voltaren<br>Amitriptyline<br>Steroid injection | Increase fall or injury was not noted. All CPK were 100% CK-MM. Investigator judged elevations as not clinically significant. |
| 0001 | Paulson | 46/F/W | -14<br>28<br>71<br>136<br>196<br>260<br>267 | | Inferior Infarct - ?; Increased cholesterol; Increased CPK; Increased eosinophils; kidney stones ?; L. knee surgery - 1987 H/A; Tight muscle - scalp;<br><br>ECG NSR; Inferior infarct age undet. | Kemidrin<br>Benadryl<br>ASA<br>Eldepryl | The CPK was already slightly increased at baseline. On Day 71, the patient complained of chest pains for which stress test was ordered. All CPK fractionizations showed ≥ 98% CK-MM. Though not clinically significant patient was referred to cardiologist. |

*Endpoint = end of study or dropout.

| PLACEBO Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments-Relevant Info |
| 0001 | Weiner | 71/F/W | -7<br>22<br>64<br>120<br>183<br>239<br>253 | | Ing hernia - 1983; Spinal fusion - 1970; R. Carpel tunnel Sx - 1993; Blood in semen - 1993; Increased CPK - etiology unknown; arthritis R. knee;<br><br>ECG Abnormal R. Waves Q II III, F; old I WMI; ST-T changes I, AV, V6 | Deprenyl-PD<br>Naproxen<br>Corticosteroid injection<br>Tetracycline<br>Dyazide | The patient's CPK was increased at baseline and remained elevated till end of study. Investigator's opinion: no evidence of skeletal muscle damage and elevation judged to be NCS. Fractionation showed ≥ 95% CK3=MM. |
| | | | | | | | |
| 0010 | Lieberman | 59/M/W | -7<br>25<br>37<br>67 | | Gastric reaction - 1966; Vagotomy-partial- 1966; Periodic back pain;<br><br>ECG = NSR | Pergolide<br>Selegiline<br>Norazepam<br>Amantadine<br>Trihexy-pheridil<br>Sinemet | Patient had increasing dyskinesia. Investigator felt the elevated CPK was secondary to severe dyskinesia which necessitated visit to ER. |



*Endpoint = end of study or dropout.

| PLACEBO Protocol: M/2730 | | | Laboratory Test: CPK (Pt's who had elevated CPK's and ret.to normal at endpoint*.) | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Bennett | 63/F/W | -11<br>25<br>32<br>53<br>109<br>170<br>221<br>228 | | Hypertension - 1992; Spinal stenosis surgery - 1992; L. Carpel tunnel syndrome surgery - 1992;<br><br>ECG-NSR, LVH by voltage | terazosin | Day 25 CPK 511; CPK fractionated showed [illegible]-MM - Contused R. wrist 3 days prior to CPK; Day 221 CPK fractionated showed CK-MM investigator comment "physical exertion" |



*Endpoint = end of study or dropout.

| PLACEBO Protocol: M/2730 | | | Laboratory Test: CPK (Pt's who had elevated CPK's and ret.to normal at endpoint*.) | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Fazzini | 65/F/W | -12<br>24<br>52<br>115<br>175<br>233<br>245 | | Angina - ASHD-63 HTN - 91; Renal calculi 1963 (nephrolithasis); L. Knee surgery - 1990; R. Ing. hernia - 1941; Tonsillectomy - 30's; Ganglion cyst R. gr. toe - 1978; Skin cyst - neck - 1978; CXR - Screen; linear scarring in R. lung field; diaphragm flattened; Aorta elongated & tortuous. Heart size enlarged - some degree of COPD & old fibrosis @ R. base ASHD suggested.<br><br>ECG - Sinus bradycardia; Early R. Wave progression; 1st degree AV block. | Eldynyl<br>Cardizem<br>Tenormin<br>ASA - nitro-glycerin | Day 24 CPK fractionated; CK-MM ; Investigator comment: NCS |
| | | | | | | | |

*Endpoint = end of study or dropout.

| PLACEBO Protocol: M/2730 | | | Laboratory Test: CPK (Pt's who had elevated CPK's and ret.to normal at endpoint*.) | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0010 | Eidelman | 46/M/W | -23<br>22<br>52<br>106<br>162<br>218<br>224 | | Diverticulitis - 1993;<br>Back pain - 1973;<br>Subarachnoid Cyst - 1990;<br><br>ECG = NSR | Sinemet CR | 1st elevation was said to be due to prolonged tourniquet time; 2nd elevation was due to patient shoveling driveway for 5 hours. Both fractionated CKB- |
| 0010 | Perimutter | 55/M/W | -7<br>29<br>43<br>99<br>155<br>213<br>218 | | Migraine - 1988; Tunnel Vision - 1990;<br>Generalized choreiform movements (brady-kinesia R>L)<br><br>ECG=NSR; L. anterior fascicular block | Persantine<br>Amantadine<br>Diphenhy-dramine<br>Sinemet CR | Patient developed severe esophageal spasm for which he was hospitalized. He also experienced increased dyskinesia & nocturnal myoclonus. The patient had multiple needle sticks prior to this blood draw accounting for elevated CPK fractionation: |

*Endpoint = end of study or dropout.

| PLACEBO Protocol: M/2730 | | Laboratory Test: CPK (Pt's who had elevated CPK's and ret.to normal at endpoint*.) | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0010 | Richter | 81/M/W | -12<br>20<br>106<br>175<br>234<br>241 | | Hypertension - 1991; L. Inguinal hernia - 1993; Back muscle spasm; Osgood-Schlatter Disease - 1993;<br><br>ECG-NSR; Slight cardiomegaly on chest x-ray | Primivil<br>Hydrochloro-thiazide<br>Toradol | Patient had elevated CPK 6 weeks prior to baseline which the investigator related to muscle trauma. Fractionation: CK3-MM = ó; Subsequently CPK came down and other fractionation also was CK3-MM : |







*Endpoint = end of study or dropout.

PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*)

| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|
| 0001 | Fazzini | 33/F/W | -7<br>22<br>53<br>92<br>148<br>162 | | ECG - Sinus bradycardia; R. bundle intraventricular conduction delay | Eldepryl<br>Permax | Day 92 CPK ,PK fractionated showed › CK-MM, Investigator comment: NCS; Day 162 dropped from study due to adverse event (paranoia & auditory hallucinations). |
| 0001 | Friedman | 60/F/W | -7<br>27<br>58<br>124<br>177<br>247<br>254 | | Hypertension, increased cholesterol; lobectomy (bronchiectasis), ulcer, IBS, hyperthyroidism; kidney stones; erectile dysfunction (due to hypertension meds); anxiety;<br><br>ECG poor R Wave progression, L. axis-clockwise rotation - ST Wave Abnormality | Eldepryl<br>Inderol<br>Mevacor<br>Zantac<br>Imodium<br>Allopurinol<br>Klonopin | Day 177 CPK CPK fractionated showed CK-MM, Investigator comment: NCS |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Kurth | 48/F/W | -16<br>22<br>50<br>101<br>154<br>224<br>230 | | Urinary urgency; head injury - 1984;<br><br>ECG - NSR | Eldepryl<br>Amantadine<br>Elavil | Day 22 CPK PK fractionated showed<br><br>Investigator comment: NCS |

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*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Olanow | 66/F/W | -2<br>22<br>50<br>**106**<br>160<br>218<br>225 | | Stroke L. - 1989; Arthritis - 1990; Intermittent constipation -1993; Back cyst removed; Mortons neuroma - 1992; Memory difficulties - 1991; Intermittent light-headedness - 1991;<br><br>ECG - Rapid early transition. Non Sp. ST-T Wave changes; Sm. non-pathological Q waves lead III. Cannot R/O old inferior posterior MI; borderline abnormalities may not indicate heart disease | Cogentin<br>Eldepryl | Prior to Day 106, Patient reported freezing; blurry vision; & increased forget-fullness; Day 106 - fractionated showed<br>Investigator comment: NCS |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Richter | 56/F/W | -5<br>51<br>107<br>170<br>247 | | Hematuria; erectile dysfunction; Rash - chest;<br><br>ECG - Sinus bradycardia; L. possible Atrial enlargement - bigeminal PAC's with standing | No relevant concomitant medications. | Day 170 CPK CPK fractionated; Shows Muscle problem ongoing per investigator |



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*Endpoint = end of study or dropout.

PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*)

| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|
| 0001 | Watts | 57/F/W | -13<br>27<br>58<br>111<br>125<br>169<br>220<br>232 | | PUD - 1972; occasional burning on urination - 1992; urinary frequency - 1992; partial amputation 5th digit R. hand - 1967; bilaterial hip pain - 1992; head trauma - 1955;<br><br>ECG sinus bradycardia L. axis deviation - old findings; T-abnormality - old findings | Selegiline<br>trinekyphe-nidyl<br>non ASA analgesic<br>ibuprofen<br>Novacaine<br>llysine | Day 111 CPK CPK fractionated; showed<br><br>Investigator comment: "No chest pain, injury or flu, will recheck again with muscle specific enzyme"; Day 125 CPK CPK fractionated showed<br><br>Investigator comment: "unknown clinical significant - asymptomatic; ? myositis; injury, without chest pain and fever; second high value will repeat and check aldolase and ESR at same time". |
| | | | | | | | |

*Endpoint = end of study or dropout.

PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*)

| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|
| 0004 | Grimes | 59/M/W | -10<br>45<br>68 | | Impotence x 1; A-Fib x 15 yrs; hypertension (renal dysfunction); transient arthritis - wrists; gout - which was drug related in 1988; cholecystecomy in 1982;<br><br>ECG Atrial Fibrilliation. | Deprenyl<br>Doxycline<br>Digoxin, ASA<br>Novahy-diazide<br>Novasen<br>Vasotec<br>Verapamil HCL<br>Selegeline<br>Isoptin<br>Enalapril Maleate | Day 45 CPK CPK not fractionated, investigator comment: "all known before". |
| 0004 | Sethi | 70/M/W | -10<br>43<br>68 | | Hiatal hernia - 1991; strained muscle mid back; benign cyst R. kidney - 1987. | Ibuprofen<br>Tums<br>Standback powder<br>amoxicillin<br>L-Deprenyl<br>Amantidine<br>Nubain<br>Fentanyl<br>Dxycodone & propexyphene | Day 43 CPK CPK not fractionated. R. hip fx - patient fell 8/2/94 @ Day 42 - hospitalized for surgery. Not walking at end of study;. |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| | | | | | | | |
| 0010 | Guttman | 52/M/O | -6<br>25<br>59<br>105<br>155<br>204<br>211 | | Kidney stone (1979)<br>MVA back injury (1989)<br>Knee effusion (1993)<br>Slightly hypertensive intermittent (L)<br>Knee pain<br>Chronic sinus infection<br><br>ECG: NSR<br>Day 56: NSR with non-specific T-wave abnormality | Sinemet CR<br>Naprosyn<br>Steroid injection (for knee) on Visit 4 Amoxicillin (for sinus) | Per investigator, the elevated CPK (not fractionated) was skeletal, probably related to osteoarthropathy & was accompanied by slight ↑ LDH (not clinically significant level o'<br>CPK levels came down at subsequent visits |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK (Pt's who had elevated CPK's and ret. to normal at endpoint.*) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0010 | Hubble | 53/M/W | -8<br>21<br>49<br>**105**<br>162<br>218<br>225 | | Multiple fractures (1961, 1962, 199)<br><br>ECG = NSR | Eldepryl<br>Trazodine<br>Restoril | Around Day 105, pt fell off a horse while riding. Investigator noted that pt. had rhabdomyolysis due to fall; fractionation was CPK subsequently returned to normal |
| 0010 | Jankovic | 62/M/W | -7<br>24<br>**43**<br>65 | | Occasional dizzy spells.<br><br>ECG = NSR | Sinemet | Pt. had complained of increasing early morning dystonia. CPK fractionation =<br><br>Pt. was discontinued from study; no work-up or diagnosis available. The CPK returned to normal on Day 65 |

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*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK ( Pt.'s who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Factor | 76/F/W | -7<br>22<br>29<br>85<br>141<br>204<br>211 | | Sm. ventral hernia midline; angina since 1975; CABG 1975; Enlarged prostate 1993; Arthritis (neck) - 1993; increased serum glucose -1989; hiatrial hernia - 1992; gall stones - 1992-93; circumcision - 1974<br><br>ECG; Sinus Rythymn borderline; 1st degree AV block; baseline artifact; systolic ejection murmur | Nitro disc<br>Ecotrin<br>Proscar<br>Eldepryl | Day 211 CPI<br>CPK fractionated showed<br>Investigator comment: NCS; No fall/injury reported. |



*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK ( Pt.'s who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Olanow | 73/F/W | -13<br>22<br>50<br>103<br>163<br>219<br>227 | | Arthritis shoulder & hip - 1983; hyper-tension - 1989; anxiety - 1973; Surgeries: Hernia - 1983; rhinoplasty - 1968; plastic surgery ears - 1958<br><br>ECG - marked sinus arrythmia - premature supraventricular complexes - occasional PAC- freq. dropped beats | Ibuprofen<br>Eldepryl<br>Zestril<br>Tranxene | Day 227 CPK [illegible] CPK fractionated; showed<br><br>Investigator comment: "minor injury?"<br>No other information available. |



*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK ( Pt.'s who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0001 | Richter | 62/F/W | -14<br>22<br>55<br>110<br>172<br>242<br>249 | | Angioplasty - 1988; histoplasmosis - 1947; appendectomy; hiatial hernia; frequency urination; enlarged prostate - 1978; mild depression; Hyper lipidemia, hypertension - 1993; anxiety - 1991;<br><br>ECG NSR; possible L. atrial enlargement; ventricular hypertrophy; ST-T Wave Abnormality; consider lateral Ischemia | Cardizen CD<br>Hytrin<br>Valium<br>Buspar<br>Benadryl<br>Tagament<br>Prozac<br>Xanax<br>Ativan | Day 249 CPK CPK fractionated showed<br><br>Investigator comment: "muscle spasm ongoing". Minor fall - Day 249. |
| | | | | | | | |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK ( Pt.'s who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0004 | Kurlan | 60/M/W | -7<br>9 | | Borderline hypertension - 1992; Arthritis; anxiety x 3 months; mild depression; hyperflexia in legs L>R;<br><br>ECG NSR movement artifact | Verapamil<br>Tylenol<br>Corimdin<br>Nitro PRN<br>Lopressor | On Day 7 patient was involved in a MVA; following syncope. While at clinic had ECG findings of ST-T wave elevations for which he was sent to ER. The diagnosis was myocardial infarction of anterior wall. Elevated CPK was not fractionated. |
| 0004 | Trosch | 63/M/W | -9<br>43<br>71 | | COPD - 1990; PVC - 1990; Hypertension - 1992; Gout - 1992; Osteoarthritis - 1992; Asthma - childhood;<br><br>ECG-NSR but possible left atrial enlargement & non-specific T-Wave Abnormality | Selegiline<br>L-deprenyl<br>Vasotec<br>dilantin<br>cyanoco-balamin<br>naproxen<br>terazosin<br>bumetanide | Day 9 - Hypertonia; Day 28 onset of bilateral pedal edema (removed from open-label study due to ongoing symptoms); Day 43 & 71 not fractionated. Investigator comment: NCS. |
| | | | | | | | |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK ( Pt.'s who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0010 | Eidelman | 63/F/W | -14<br>24<br>46 | | CABG (1990); AAA repair; Duodenal ulcer (1994); Fx - R shoulder (1992); knee replacement (1993); Obese; slightly hypertensive;<br><br>ECG: Sinus tachycardia; L anterior fascicular block | Permax<br>Parlodel<br>Lasix<br>Eldepryl<br>K-Dor | Pt. fell several days prior to Day 46; CPK was not fractionated; pt. dropped from the study on Day 46 due to adverse event (visual hallucination) |
| 0010 | Paulson | 64/M/W | -12<br>23<br>92<br>148 | | Dementia (1987);<br>Hallucination (1990)<br>Leg cramps (1989)<br>Thrombosed hemorroids<br><br>ECG: NSR | Sinemet CR<br>Symmetrel<br>Florinef<br>(started on Day 90) | Around Day 148 - the ECG showed "old inferoposterior infarction". According to investigator, the patient had silent infarct & family doctor notified. Pt. died unexpectedly in his sleep. |

*Endpoint = end of study or dropout.

| PRAMIPEXOLE Protocol: M/2730 Laboratory Test: CPK ( Pt.'s who had elevated CPK's at endpoint*). | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study # | Patient # Investigator | Age/Sex /Race | Day of Study | CPK Value U/L | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
| 0010 | Tetrud | 60/F/W | Baseline<br>20<br>51<br>107<br>163<br>191<br>212 | Not done | Hypertension (1982)<br>Hypothyroid (46 years)<br>Arthritis (1982)<br>Dystonia (foot, 1986)<br>Depression (1993)<br><br>ECG: NSR<br>Chest X-ray:<br>Mild scarring & atelectasis (Both bases - not clinically significant.) | Parlodel<br>Triam/Hcz<br>Synthroid<br>Ecotrin<br>Sinemet<br>Flexeril (for dystonia) | Pt. had complained of increased shakiness, stiffness, tremor & worsening dystonia in spite of Flexeril; the dystonia was moderate to severe at times; CPK fractionated on Day 191 & 212. Showed |

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*Endpoint = end of study or dropout.

**Table 2 Placebo: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0001 | Watts | 58/F/W | | | | | -12<br>24<br>51<br>113<br>124<br>170<br>229<br>235 | | borderline hypertension, bilateral ankle edema, gallstone, kidney stone, L. pyelolithotomy, R. knee pain, insomnia, dry mouth, voice hoarseness, H/As, urinary hesitation urgency, EKG - NSR with sinus arrhythmia - R. ventricular conduction delay - old findings, asymptomatic - sinus bradycardia | l-deprenyl, Rolaid, nizoral, ibuprofen, bufferin, Maalox | bilirubin wnl thru out study, SGPT & GGT increased at visit 13, inv. comment "clinically significant - was mildly symptomatic x 1 day with midline abd. pain, ? gallstone passed - recheck lab next wk, has had history of gallstones in past". GGT increased at visit 14 - inv. comment "NCS - prob. gallstone effect again" |
| 0001 | Farmer | 64/F/W | | | | | -7<br>23<br>51<br>107<br>163<br>219<br>226 | | old knee inj, L. traumatic pinoveal nerve (same as muscular), mild depression - occ. bouts, back surgery - disc, PX: L. foot drop, CXR - mild atherosclerotic CV changes, degenerative mid-thoracic spine changes, hilar promenence is considered to be due to pulmonary vessels | Sinemet, sulfamethoxazde, doxycycline, Hytrin, urispas, Motrin | bilirubin wnl thru out study, GGT increased at screen - inv. comment "NCS - other LFT is OK - will f/u during trial" prostatitis at visit 10 |

*Patients with ≥ 2 increased LFT abnormalities.



(Continued)

**Table 2 Placebo: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0004 | Trosch | 56/M/W | | | | | -9<br>43<br>71 | | bladder infections, osteoarthritis/hands, muscular H/A, transient vocal cord paralysis, abd. umbilical hernia, occasional insomnia, depression, chemical pneumonia due to epoxy paint,1970 PX: umbilical hernia, high frequency hearing loss | l-deprenyl, Mylanta, fluoxetine, ibuprophen, diphendydramine, pseudoephidrine, excedrin x 2 days for H/A (day 42) | bilirubin wnl thru out study, GTT elevated day inv. NCS |
| 0010 | Karp | 72/M/W | | | | | 5<br>37<br>59<br>115<br>173<br>236 | | post nasal drip (hayfever), appendectomy, CXR - mild COPD | Symmetrel, Sinemet, ASA, chlortrimeton | bilirubin wnl thru out study, GGT increased at screen - labs repeated at visit 1, GGT increased - inv. comment "probably 2° to sinemet high-dose, visit 2 - hematuria - ref. to urologist & primary care phy., cystoscopy & IVP - mass R. kidney (no f/u req) |

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**Table 2 Placebo: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Guttman | 62/M/W | | | -14<br>23<br>49<br>94<br>141<br>206<br>212 | | | | atrial fibrillation - intermittent, congestive heart failure, seasonal asthma, hayfever, cholecystectomy, inguinal hernia repair, abn. liver function tests, diabetic, back pain, prostate surgery, bladder volume small - surgical expansion, hydronephrosis - partial; PX: R. arm mole (no change at end of study), EKG non-specific ST-T, changes possible old inferior infarct - incomplete R. bundle branch block | symmetrel, flexeril, glyburide, lanoxin, lasix, asprocream, instantine, prolopa, psyllium, nitropatch | bilirubin wnl thru out study, SGOT, SGPT increased - inv. states "chronic elevation flucuating abnormaly in past" - NCS, EKG changed from baseline at visit 19 - possible ischemia noted, f/u with FMD next day - on $O_2$ (1 liter) at noc for dyspnea, study drug D/C until cardiac evaluation is completed visit 19 |

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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0001 | Farmer | 77/F/W | | | | | -9<br>22<br>50<br>79<br>89 | | hypertension, cholecyst-ectomy, menopause, inguinal herniorrhaphy, multi infarct dementia with short term memory loss, cataract surgery, Px - mild thyroid enlargement, no mass, +1 ankle edema, occ. ecchymotic areas, EKG - marked sinus arrhythmia with sinus bradycardia, occ. supra-ventricular complexes | Trental, Norvasc, Kerlone, Darvocet | NCS, bilirubin wnl thru out study, GGT increased - NCS/inv. |
| 0001 | Siemers | 59/F/W | | | | | -14<br>22<br>43<br>92<br>148<br>204<br>211 | | peptic ulcer disease - melena approx. twice/year, cholecystectomy, intermittant H/A, mild L. ulnar neuropathy, bilateral foot pain/planter callouses, CXR abn. - calcified granuloma RUL, | l-deprenyl, Tagamet, Tylenol, v-cillin, Baclofen, mylanta, ASA - (Baby), gaviscon, Valium, Ex-lax, inderal, benadryl, Clariton | bilirubin wnl thru out study, SGPT & GGT increased at screen - inv. comment "prior common bile duct stint following transection during cholecystectomy, clinically aymptomatic for 20+ years NCS", onset of hypertension at visit 17 |

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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0001 | Siemers | 67/F/W | | | | | -14<br>22<br>29<br>85<br>139<br>197<br>204 | | hypertension, CAD, allergy - voltarin, hayfever, colitis, bowel obstruction - surgery, diabetes, hypothyroidism, fibromyalgia, bursitis both shoulders, anxiety, idiopathic thrombocytopenic purpura, cataracts - bilateral, gastroesophageal reflex,<br>CXR - abn. - area of atelectasis bi-apical pleural thickening, inv./NCS,<br>EKG - L. atrial abn. NSR,<br>PX: +1 pedal edema | l-deprenyl, premarin, Verelan, Provera, Xanax, Beconase AQ, Synthroid, Darvocet, Artane, Mylanta, titralac acid, carafate | bilirubin wnl thru out study, GGT increased - "Estrogen replacement" NCS per inv. |
| 0004 | Kurlan | 60/M/W | -7<br>9 | 19<br>173 | | | | | borderline hypertension, ragweed allergy, arthritis, anxiety x 3 months, mild depression, PX: hyper-reflexia in legs L>R,<br>EKG - Abn Q waves V1 - V6 st. elevation V1 - V6, extensive acute anterior wall injury/MI | acetomenophen, Verapamil | bilirubin elevated day 70 but remained within predefined limits - pt. was having myocardial infarction - increased CPK at the time of lab draws day 70, pt. terminated from study week 10 (day 70) |

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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0004 | Hurtig | 50/F/B | | | | | -16<br>53<br>76 | | hypertension, diabetes, sciatica - left, hepatitis (comment: GGT levels as high as 660 per FMD) | l-deprenyl, ibuprophen, insulin | bilirubin values normal thru out study, GGT values elevated thru out study - investigator indicates not significant due to history of hepatitis, episodic headaches during study-relieved with Motrin |
| 0004 | Trosch | 67/M/W | | | | | -14<br>43<br>71 | | systolic murmur, episodic pulmonary inf, allergy - pcn, Ca Prostate - "93"/ Surgery 93, Fx R. wrist - 47; arthritis R & L shoulders, melanoma & surgery L. shoulder - 1991, head trauma - 1957, Fx L. ankle - 89, T&A, hemorrhoids & surgery, cataract & surgery - 1990, facial/plastic surgery, EKG - bradycardia - L. Axis deviation with occ PVC. | l-deprenyl, Tavist-D, clindamycin (prophylatic finger infection) | bilirubin wnl thru out study, GGTincreased - NCS by inv., URI - day 70 |

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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments-Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Eidelman | 67/F/W | -6<br>23<br>51<br>94<br>148<br>204<br>209 | | -6<br>23<br>51<br>94<br>148<br>204<br>209 | | -6<br>23<br>51<br>94<br>148<br>204<br>209 | | cardiac cath - 50% blockage of L. decending artery, hypertension, PVC's (normal EKG), allergy - pcn, sulfa, hiatal hernia with esophageal reflux, cholecystectomy, hypothyroid, hypercholestendemia, c-section, ruptured ectopic preg, arthritis, sciatica, stapedectomy L. ear, deaf L., anxiety | Symmetrel, Synthroid, Maalox, Bentyl, Cogentin, Zantac, Ascriptin, eldepryl, Xanax, Sinemet, Cardizen, Senokot, tetracycline | bilirubin wnl thru out study, Dx of common bile stenosis by internist at visit 14, increased LFTs - inv. "referred to internist for flu", numbness across upper lip visit 10, carotid & transcranial doppler were ordered |



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*Patients with ≥ 2 increased LFT abnormalities.
+Patients with elevated LFT but returned to normal at endpoint.



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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Golbe | 74/F/W | | | -21<br>29<br>85<br>141<br>199<br>206 | | | | hypertension, hysterectomy, R. ankle pain, depression, insomnia, cataract removed - OD, Px - LUE numbness, loud $S_4$ RSB, EKG: NSR L. Axis deviation - possible anterior infarct age undetermined,non-specific T wave abnormality, non-specific ST abnormality anterior leads, CXR - small nodule L. upper lung field, no change from old films | Diazepam, trazodone, Ambien, temazepam, chlorthalidone, Sinemet, Tylenol | SGOT, SGPT, GGT increased - inv. comment "will watch - chronic & recurrent", bilirubin wnl thru out study |
| 0010 | Factor | 49/M/W | -7<br>22<br>29 | | | | | | valve disease (aortic) replacement, hypertension, asthma, peptic ulcer, ruptured appendix - bowel resection, osteoarthritis, depression, herniorrhaphy, vein stripping/varicose veins, EKG - sinus tachycardia, CXR cardiomegaly - NCS | Klonopin, Motrin, Sinemet, Baclofen, Colace, Benadryl, Prozac, Ventolin spray, Permax, chloralhydrate | visit 5 increased SGOT inv. comment "Dx with rhabdomyolysis", hospitalized visit 9 due to increased CK mm, bilirubin wnl thru out study |

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+Patients with elevated LFT but returned to normal at endpoint.



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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Paulson | 64/M/W | -12<br>23<br>36<br>92<br>148 | | | | | | shingles, dementia, hallucinations, old thrombosed hemorrhoid L. lateral quadrant, leg cramps, light headed, PX: dementia & hallucinations, CXR - plaque-like disease probably related to asbestos, EKG - sinus arrthymia & junctional ST depression old, inferoposterior infarction | Symmetrel, Florinef, Sinemet CR, thiamine, Zofran | bilirubin wnl thru out study, SGOT increased visit 16, inv. comment "He had, apparently, a heart attack". Pt. was asymptomatic - died unexpectedly at night. |
| 0010 | Friedman | 72/F/W | | | | | -7<br>24<br>57<br>108<br>162<br>218<br>225 | | hypertension, congestive heart failure, allergy to some medications, gallbladder out, low back strain, clinical myelopathy, depression, R. mastectomy, CA colon - resection, insomnia, hypotonic bladder, Px - +2 pedal edema, EKG NSR - possible anteroseptal infarct non-specific, ST-T wave abnormalities | lanoxin, Sinemet CR, Pamelor, Benadryl, Restoril, Valisone Cream, Tylenol, quinine, Lasix | GGT increased - NCS, bilirubin wnl thru out study, mod to severe bilateral leg pain visit 6 to end of study |



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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Jankovic | 45/M/W | | | -7<br>24<br>78<br>136<br>194<br>204 | | -7<br>24<br>78<br>136<br>194<br>204 | | possible history of murmur, eczema, lumbar laminectomy, post traumatic stress inj, EKG L. axis deviation, early precardial R/S transition, sinus tachycardia, Px: eczema - face | e-ldepryl, Sinemet, amitriptyline, tums, Voltarin, Betametasone, Advil | bilirubin wnl thru out study, inv. made no comments re. increased LFTs |
| 0010 | Montgomery | 65/F/W | | | | | -7<br>22<br>50<br>73 | | Pt. has had increased LFTs for many years, post-menopausal, R. mastectomy | Sinemet, Gyne Lotrimin Vaginal Cream | GGT increased - inv. "NCS - known for sometime", bilirubin wnl thru out study, pt. withdrawn from study due to paranoia visit 19 |



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*Patients with ≥ 2 increased LFT abnormalities.



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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments-Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Richter | 67/M/W | | | -7<br>22<br>50 | | -7<br>29<br>50 | | intermittent hypotensive episodes, constipation, kidney stones x 3 - surgery x 3 ultrasound x 2, impotence, skin cancers - removal, EKG - NSR with occ. premature supra-ventricular complexes, L. anterior fasicular block, CXR - small area discord atelectasis at L. base otherwise essentially normal chest | e-ldepryl, Donnatal, Sinemet, lortab | abn. hepatic function at visit 5 - hepatitis eval. I done for increased LFTs, pt. positive for A, AB, bilirubin remained wnl thru out study & pt. remained asymptomatic, study meds stopped due to abn hepatic function & pt. allowed into open label when LFT ret. to normal |

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*Patients with ≥ 2 increased LFT abnormalities.



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**Table 1 Pramipexole: Patients with Elevated LFTs (Outside Pre-defined Limits)**

Adequate & Well-Controlled Studies

Protocol: M/2730

| Study # | Patient # Investigator | Age/ Sex/ Race | SGOT U/L | | SGPT U/L | | GGT U/L | | Relevant Medical History & Physical Findings | Concomitant Medication | Investigator Comments- Relevant Info |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Day of Study | Value | Day of Study | Value | Day of Study | Value | | | |
| 0010 | Stoessl | 68/F/W | | | | | -14<br>23<br>52<br>105<br>161<br>217<br>224 | | hypertension, allergy - sulfa, appendectomy, cholecystectomy, Fx R. femur - internal fixation, arthritis, occasional nocturnal visual hallucinations, no frank psychosis, levodopa related, macular degeneration, sciatrica, PX: GRII/VI murmur, osteoarthritic knees,<br>CXR - cardiomegaly - questionable density, lingular lobe on the left - etiology unk,<br>EKG NSR nondiagnostic inferior ST, depression - incomplete L. BBB, sinus tachycardia L. axis deviation, echo cardigram scheduled due to one episode of chest pain | Domperidone, Dulcolax, surgam, amitriptyline, calcium carbonate, Sinemet, Tylenol #2, fluviral | bilirubin wnl thru out study, increased GGT - inv. comment "repeated and judged not to be clinically significant" |





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