

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: 020667**

**ADMINISTRATIVE DOCUMENTS**

**PRAMIPEXOLE TABLETS NDA 20-667**

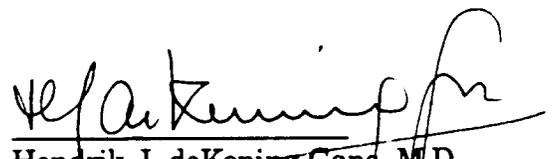
**XIII. PATENT INFORMATION**

**PATENT CERTIFICATION**

1.	Active Ingredient	Pramipexole
2.	Strength(s)	0.125, 0.25, 1.0, 1.25 and 1.5 mg
3.	Trade Name	To be determined
4.	a. Dosage Form	Compressed Tablets
	b. Route of Administration	Oral
5.	Applicant Firm Name	The Upjohn Company
6.	NDA Number	20-667
7.	NDA Approval Date	To be determined
8.	Exclusivity - Date first ANDA could be approved and length of exclusivity period	Five (5) years after date of NDA approval / December 12, 2006 / or date of any patent extension -- whichever date occurs last.
9.	Applicable patent numbers and expiration date of each	4,886,812 - compound patent Expiration date - December 12, 2006  4,843,086 - use in Parkinson's disease Expiration date - June 27, 2006

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ON ORIGINAL

This is to certify that the above information is correct to the best of my knowledge.

  
Hendrik J. deKoning Gans, M.D.  
Regulatory Liaison

EXCLUSIVITY SUMMARY for NDA # 20-667 SUPPL # \_\_\_\_\_

Trade Name Mirapex<sup>®</sup> Generic Name Pramipexole Tablets 0.125; 0.25; 1.0; 1.25; & 1.5 mg.

Applicant Name Pharmacia & Upjohn HFD- 120

Approval Date \_\_\_\_\_

**PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?**

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it an original NDA? YES / X / NO / \_\_\_ /

b) Is it an effectiveness supplement? YES / \_\_\_ / NO / X /

If yes, what type? (SE1, SE2, etc.) \_\_\_\_\_

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES / X / NO / \_\_\_ /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

\_\_\_\_\_  
\_\_\_\_\_

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

\_\_\_\_\_  
\_\_\_\_\_

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d) Did the applicant request exclusivity?

YES /  / NO /  /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5

**IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.**

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?

YES /  / NO /  /

If yes, NDA # \_\_\_\_\_ Drug Name \_\_\_\_\_

**IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.**

3. Is this drug product or indication a DESI upgrade?

YES /  / NO /  /

**IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).**

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**PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /    / NO / X /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # \_\_\_\_\_  
NDA # \_\_\_\_\_  
NDA # \_\_\_\_\_  
NDA # \_\_\_\_\_  
NDA # \_\_\_\_\_

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /    / NO /    /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # \_\_\_\_\_  
NDA # \_\_\_\_\_  
NDA # \_\_\_\_\_

**IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES," GO TO PART III.**

**PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS**

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /\_\_\_/ NO /\_\_\_/

**IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.**

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /\_\_\_/ NO /\_\_\_/

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If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:**

\_\_\_\_\_  
\_\_\_\_\_

- (b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES / \_\_\_ / NO / \_\_\_ /

- (1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES / \_\_\_ / NO / \_\_\_ /

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

- (2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES / \_\_\_ / NO / \_\_\_ /

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # \_\_\_\_\_

Investigation #2, Study # \_\_\_\_\_

Investigation #3, Study # \_\_\_\_\_

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- c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #\_\_, Study # \_\_\_\_\_

Investigation #\_\_, Study # \_\_\_\_\_

Investigation #\_\_, Study # \_\_\_\_\_

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

- a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # \_\_\_\_\_ YES / \_\_\_ / ! NO / \_\_\_ / Explain: \_\_\_\_\_

Investigation #2

IND # \_\_\_\_\_ YES / \_\_\_ / ! NO / \_\_\_ / Explain: \_\_\_\_\_

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- (b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES / \_\_\_ / Explain \_\_\_\_\_

NO / \_\_\_ / Explain \_\_\_\_\_

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Investigation #2

YES /    / Explain \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_

NO /    / Explain \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /    / NO /    /

If yes, explain: \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

  / S /   \_\_\_\_\_  
Signature \_\_\_\_\_ Date   11/20/96    
Title:   FMO  

  / S /   \_\_\_\_\_  
Signature of Division Director \_\_\_\_\_ Date   7/1/97  

Approved this day

cc: Original NDA    Division File    HFD-85 Mary Ann Holovac

# PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NDA # 20-667

Supplement #      Circle one: SE1, SE2, SE3, SE4, SE5, SE6

HFD-120 Trade (generic) name/dosage form: Mirapex (Pramipexole) Tablets Action: AP AE NA

Applicant Pharmacia & Upjohn Therapeutic Class 1S

Indication(s) previously approved: None

Pediatric labeling of approved indication(s) is adequate  inadequate  *Drug is intended*

Indication in this application:

*largely for elderly population; no use yet in pediatric population.*

(For supplements, answer the following questions in relation to the proposed indication.)

- 1. **PEDIATRIC LABELING IS ADEQUATE.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric subgroups. Further information is not required.
- 2. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.
  - a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.
  - b. The applicant has committed to doing such studies as will be required.
    - (1) Studies are ongoing.
    - (2) Protocols were submitted and approved.
    - (3) Protocols were submitted and are under review.
    - (4) If no protocol has been submitted, explain the status of discussions on the back of this form.
  - c. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.
- 3. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in children. Explain, on the back of this form, why pediatric studies are not needed.
- 4. **EXPLAIN.** If none of the above apply, explain, as necessary, on the back of this form.

EXPLAIN, AS NECESSARY, ANY OF THE FOREGOING ITEMS ON THE BACK OF THIS FORM.

/S/

Dir OBE

Signature of Preparer and Title (PM, CSO, MD, other)

APPROVE THIS WAY

ON ORIGINAL

7/1/97

Date

cc: Orig NDA  
HFD-120/Div File  
NDA Action Package  
HFD-510/GTroendle (plus, for CDER APs and AEs, copy of action letter and labeling)

APPROVE THIS WAY  
ON ORIGINAL

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

**DEBARMENT CERTIFICATION FOR NDA 20-667****Pramipexole Tablets**

Pursuant to section 306(k)(1) of the Federal Food, Drug and Cosmetic Act, the applicant certifies that, to the best of its knowledge and belief, the applicant did not and will not use in any capacity the services of any person listed pursuant to section 306(e) as debarred under subsections 306(a) or (b) of the Act in connection with this application.



Ann L. Buckley  
Executive Director,  
Worldwide Regulatory Compliance

18 Dec 95

Date

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

11041  
~~CONFIDENTIAL~~

MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: July 12, 1996

FROM: Paul Leber, M.D., Director  
Division of Neuropharmacological Drug Products, HFD-120

RETURN

AUG 26 1996

SUBJECT: Request for Assessment of a Trademark for a Proposed Drug Product

TO: Daniel Boring, Chair  
Labeling and Nomenclature Committee  
HFD-600, Metropark North II

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Proposed Trademark: MIRAPEX (Pramipexole) Tablets NDA 20-667

Established name, including dosage form: Pramipexole Tablets

0.125, 0.25, 1.0  
1.25, 1.5

Other trademarks by the same firm for companion products: None

Indications for Use (may be a summary if proposed statement is lengthy):

treatment of the signs and symptoms of idiopathic Parkinson's disease

Initial comments from the submitter: (concerns, observations, etc.)

See attached copies of the "Description, Indications and Usage, Overdosage, and Dosage and Administration" Sections of the package insert.

Any questions call Jack Purvis, 4-5525.

cc: ORIG NDA 20-667, HFD-120, HFD-120/SBlum/Zarifa, HFD-120/JPurvis/rd4/22/96

/S/  
7/12/96

APPEARS THIS WAY  
ON ORIGINAL

Consult #641

MIRAPEX

pramipexole tablets

The LNC noted the following look alike/sound alike conflicts with the trademark: MIRASEPT (OTC contact lens solution) and minaprine (antipsychotic unavailable in the U.S.) however, the Committee believes there is a low potential for confusion with these names given the different storage environments for each product. The Committee found no misleading or fanciful aspects in the proposed proprietary name.

The Committee has no reason to find the proposed name unacceptable.

/S/ 8/22/96, Chair  
CDER Labeling and Nomenclature Committee

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL