

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

**APPLICATION NUMBER: NDA 21-335**

**ADMINISTRATIVE DOCUMENTS**

## Patent Submission

### Time Sensitive Patent Information

Pursuant to 21 C.F.R. 314.53

for

NDA # 21-335

The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

- Trade Name: \_\_\_\_\_
- Active Ingredient(s): imatinib mesylate
- Strength(s): 50 mg, 100 mg
- Dosage Form: Capsule
- Approval Date: Pending

#### A. This section should be completed for each individual patent

**U.S. Patent Number:** 5,521,184

**Expiration Date:** May 28, 2013

**Type of Patent—Indicate all that apply:**

- |   |           |           |
|---|-----------|-----------|
| 1. Drug substance (Active Ingredient)     | <u>✓Y</u> | <u>N</u>  |
| 2. Drug Product (Composition/Formulation) | <u>✓Y</u> | <u>N</u>  |
| 3. Method of Use                          | <u>Y</u>  | <u>✓N</u> |

- a. If patent claims method(s) of use, please specify approved method(s) of use or method(s) of use for which approval is being sought that are covered by patent:

**Name of Patent Owner:** Novartis AG

**U.S. Agent (if patent owner or applicant does not reside or have place of business in the US):**

#### B. The following declaration statement is required if any of the above listed patents have Composition/Formulation or Method of Use claims.

The undersigned declares that the above stated United States Patent Number 5,521,184 covers the composition, formulation and/or method of use of imatinib mesylate (STI571). This product is:

- Currently approved under section 505 of the Federal Food, Drug,

\_\_\_\_\_ and Cosmetic Act)  
or

- the subject of this application for which approval is being sought.)

Signed:   
Michael U. Lee

Title: Patent Attorney

Date: January 11, 2001

Telephone Number: 908) 522-6794

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A copy of the above information should be submitted to the NDA with the original application or as correspondence to an existing NDA. For patents issued after the NDA is filed or approved, the applicant is required to submit the information within 30 days of the date of issuance of the patent.

To expedite publication in the *The Orange Book*,\* a deskcopy should be submitted to:

Mailing address: (US Mail)

U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Data Management and Services  
Information Services Team  
HFD-93  
5600 Fishers Lane  
Rockville, MD 20857

OR

Location address: (for FedEx deliveries)

U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Data Management and Services  
Information Services Team  
Building A  
HFD-93 Room #235  
Nicholson Lane Research Center  
5516 Nicholson Lane  
Kensington, MD 20895

OR faxed to: (301)-594-8463

\* - Please note that patents for unapproved compositions, formulations, or uses will NOT be published in the *The Orange Book*.

EXCLUSIVITY SUMMARY for NDA # 21-335 SUPPL # \_\_\_\_\_

Trade Name Gleevec Generic Name imatinib mesylate

Applicant Name Novartis Pharmaceuticals Corporation HFD- 150

Approval Date May 10, 2001

**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 /  / NO /  /

b) Is it an effectiveness supplement? YES /  / NO /  /

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 /  / 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:  
\_\_\_\_\_  
\_\_\_\_\_

d) Did the applicant request exclusivity?

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

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

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e) Has pediatric exclusivity been granted for this Active Moiety?

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

**IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

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? (Rx to OTC Switches should be answered No - Please indicate as such).

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

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

**IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

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

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

**IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).**

**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 # \_\_\_\_\_

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 /\_X\_/

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 9. 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 9.

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 /\_\_\_/

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 9:**

\_\_\_\_\_

\_\_\_\_\_

- (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 # \_\_\_\_\_

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /\_\_\_/ NO /\_\_\_/

Investigation #2 YES /\_\_\_/ NO /\_\_\_/

Investigation #3 YES /\_\_\_/ NO /\_\_\_/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

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

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1                      YES /\_\_\_/                      NO /\_\_\_/  
 Investigation #2                      YES /\_\_\_/                      NO /\_\_\_/  
 Investigation #3                      YES /\_\_\_/                      NO /\_\_\_/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

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

(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: \_\_\_\_\_  
! \_\_\_\_\_  
! \_\_\_\_\_  
!

(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 \_\_\_\_\_  
! \_\_\_\_\_  
! \_\_\_\_\_  
!

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/**

Ann Staten  
Signature of Preparer  
Title: Regulatory Health Project Manager

\_\_\_\_\_  
Date

**/S/**

Richard Pazdur, M.D.  
Signature of Office or Division Director

\_\_\_\_\_  
Date

CC:  
Archival NDA  
HFD- /Division File  
HFD- /RPM  
HFD-093/Mary Ann Holovac  
HFD-104/PEDS/T.Crescenzi

Form OGD-011347  
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

FDA Links Searches Check Lists Tracking Links Calendars Reports Help

**PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)**

[View as Word Document](#)

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NDA Number: 021335 Trade Name: IMATINIB MESYLATE)50/100MG CAPS  
 Supplement Number: 000 Generic Name: IMATINIB MESYLATE  
 Supplement Type: N Dosage Form:  
 Regulatory Action: OP COMIS Indication: TREATMENT OF CHRONIC MYELOID LEUKEMIA  
 Action Date: 2/27/01

Indication # 1 accelerated phase, blast crisis and interferon refractory CML  
 Label Adequacy: Does Not Apply  
 Formulation Needed: Other  
 Comments (if any): 4-16-01 Pediatric Rule does not apply to Orphan Designated Drugs

Ranges for This Indication

<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
Adult	Adult	Waived	

— Comments: Orphan Drug

This page was last edited on 4/16/01

\_\_\_\_\_  
 Signature *ISI*

\_\_\_\_\_  
 Date *4/16/01*

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commercial

information

NDA No. 21-335

(imatinib mesylate) Capsules  
New Drug Application

**NOVARTIS CERTIFICATION  
IN COMPLIANCE WITH THE  
GENERIC DRUG ENFORCEMENT ACT OF 1992**

NOVARTIS PHARMACEUTICALS CORPORATION certifies that it did not and will not use in any capacity the services of any person debarred under section 306(a) or 306(b) of the Federal Food, Drug and Cosmetic Act in connection with this application.

Feb. 23, 2001  
Date

Ellen Cutler  
Ellen Cutler  
Associate Director  
Drug Regulatory Affairs

## TELECON MINUTES

**TELECON DATE:** May 2, 2001 **TIME:** 8:30 **LOCATION:** B

**NDA:** 21-335 **preparation documents:** FDA fax 4-30-01  
Sponsor E-Mail 5-1-01

**DRUG:** Gleevec (imatinab mesylate) **INDICATION:** CML

**APPLICANT:** Novartis **TYPE of TELECON:** Labeling

**FDA PARTICIPANTS:** Grant Williams, M.D., Medical Team Leader, HFD-150  
Martin Cohen, M.D., Medical Officer, HFD-150  
Dotti Pease, Project Manager, HFD-150

**INDUSTRY PARTICIPANTS:** Bob Miranda, Reg. Affairs, Novartis  
Elizabeth Vell, Stat., Novartis Basel  
Renoud Captivil, Clin. Novartis Basel  
Insa Gopfman, Novartis Basel

**MEETING OBJECTIVES/BACKGROUND:** Discuss FDA's 4-30-01 fax (especially comment #1 re: response rates) and general comments on E-Mailed latest version of Novartis labeling.

### DISCUSSION:

1. FDA's 4-30-01 fax requested a change in the MCyR from 21% to . . . . . After discussion, everyone concurred it should remain 21%. However, FDA's breakdown of complete (CR) vs. partial response (PR) is 7 and 14 in contrast to Novartis' 14 and 7 respectively. The medical review team will discuss this table and send Novartis a proposal.
2. Re: item #2 of the fax, Novartis is re-doing their adverse events (AE) table to include all AEs, not just drug-related AEs.
3. General labeling comments:

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•  
DRAFT LABELING

DRAFT Labeling  
covit

**ACTION ITEMS:**

1. Novartis to send updated AE table today.
2. FDA to get comments on labeling to Novartis late today.
3. FDA to get final draft labeling to Office and Novartis on Friday. The Office may make revisions and may also not agree with accelerated approval for all 3 indications.

APPEARS THIS WAY  
ON ORIGINAL

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information

Office of Post-Marketing Drug Risk Assessment  
HFD-400; Rm. 15B03  
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: April 16, 2001  
NDA NUMBER: 21-335  
NAME OF DRUG: ( ) (imatinib mesylate) Capsules, 50 mg and 100 mg  
NDA HOLDER: Novartis Pharmaceuticals Corporation

I. INTRODUCTION:

This consult was written in response to a request from the Division of Oncology Drug Products (HFD-150) for assessment of the tradename ( ) The sponsor contracted with the Institute for Safe Medication Practices (ISMP) to produce two Med-ERRS evaluations.

OPDRA's initial review of ( ) was completed on March 29, 2001 and was found unacceptable due to the potential for confusion with the existing drug *Glyset*.

PRODUCT INFORMATION

( ) is a protein-tyrosine kinase inhibitor. It is indicated for the treatment of patients with chronic myeloid leukemia in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy. ( ) is available in 50 mg and 100 mg hard gelatin capsules.

II. RESPONSE TO THE SPONSOR'S APPEAL:

1. Sponsor's Comments:

Novartis will ship supplies of ( ) in a controlled manner. There will be no automatic shipments of ( ) made to retail pharmacies. For a variety of reasons, among them a relatively small chronic myeloid leukemia (CML) patient population of approximately 23,000 individuals, Novartis has identified a number of select wholesalers that have the technical capability and resources to provide patient-specific delivery service to retail pharmacies on an as needed basis. These wholesalers will maintain inventories of ( ) and will provide adequate patient service at the retail level without the need for retail pharmacies to maintain shelf inventories of ( ) Consequently, we believe that the absence of shelf inventories of ( ) at the retail level essentially eliminates the potential for confusion with *Glyset*, a product that is not widely used in the management of diabetes. The reported new prescriptions written for *Glyset* is very low and is reported at about an average of ( ) per month since its launch in Feb 1999.

*OPDRA's Comments:*

Even though ( ) is geared towards a small population and is ordered on an "as needed" basis, pharmacies may order the drug ahead of the next prescription so that if the patient is suddenly out of the medication, he or she will not have to wait another day to receive the medication. In this case, the drug product would be placed on the shelf in close proximity of the *Glyset* product. However, the source of the potential confusion does not lie on whether or not the product is on the shelf, but whether there is a potential error made by practitioners in prescribing the medication or by pharmacists who may interpret the *Glyset* as ( ) or vice versa. A limited distribution of ( ) does not prevent the practitioner from verbally communicating the wrong prescription to the pharmacist.

Of great concern is the patient's exposure to the dangerous side effects if ( ) was given instead of *Glyset*. Such dangerous side effects include neutropenia and thrombocytopenia.

2. *Sponsor's Comments:*

A visual comparison between ( ) and *Glyset* shows a number of distinctions between the two products that should reduce the likelihood of confusion at the pharmacy and patient level. *Glyset* is available as 25 mg, 50 mg and 100 mg white, round, film-coated tablets. These tablets are debossed with the word "Glyset" on one side and the strength on the other side. ( ) will be marketed as a light yellow to orange yellow opaque capsule in a 100 mg strength, with an imprinted alpha-numeric code. These visual distinctions should allow patients to immediately identify any difference during prescription refills.

*OPDRA's Comments:*

The differences in the physical appearances of ( ) and *Glyset* are not relevant in this case since the source of error exists in the interpretation of the name when the prescription is given by the practitioner to the pharmacist. The two names have sound-alike qualities where the prefix (Gli with the long "i" and Gly) and the suffix (ec and et) sound similar. Both have an overlapping strength and the same route of administration. These similar qualities increase the potential for medication errors to occur. Of one concern noted from the Med-ERRS study is the pronunciation of "Glyvek" (glee' vek) which prompted a hit for *Glyset*. However, the look-alike similarity between these two names are stronger than the sound-alike similarity since "glee" and "gly" sound different.

Post-marketing experience with the drug product "Celebrex" has demonstrated that having *noteworthy differences between products does not eliminate* the potential error, as the Agency has received 116 reported cases of medication errors involving Celebrex, Celexa, and Cerebyx. Celebrex is an NSAID, cox-2 inhibitor indicated for the relief of the signs and symptoms of osteoarthritis and rheumatoid arthritis. Celexa is a serotonin reuptake inhibitor indicated for the treatment of depression. Cerebyx is a prodrug and its active metabolite is phenytoin. Table 1 describes the FDA approved dosage forms, strengths, and usual dosages of each product. Celebrex and Cerebyx share none of the common factors mentioned above, and, therefore, one would perceive that these three drug products would never be confused. Also, the only commonality that Celebrex and Celexa share is a dosing interval of once daily. The only *common factor* that these names share is the *sound-alike and look-alike properties of their names*.

TABLE 1

Name of Drug	Available Strength and Dosage Form	Usual Dosage
Celebrex	100 mg and 200 mg Capsules	200 mg once daily or 100 mg to 200 mg twice daily
Cerebyx	50 mg PE/mL Injection 10 mL and 2 mL vial	Varies depending on indication. Average of 10-20 mg PE/kg
Celexa	20 mg and 40 mg Tablets	20 mg to 40 mg once daily. Up to 60 mg daily

Therefore, based on previous post-marketing experience, OPDRA does not believe that differences such as differentiating dosage forms, different routes of administration, different doses, and different indications rule out any potential for confusion when the names clearly sound or look alike to a currently marketed drug product. The errors for Celebrex are not overwhelmingly related to other confounding factors such as illegible handwriting, overlapping indications for use, overlapping strengths, mispronunciation of the product names, similar prescribing environments but rather to a cognitive error. It is evident from the case reports that the sound-alike/look-alike properties of the name alone are not the source of confusion in the minds of healthcare providers. The reports describe healthcare providers thinking, seeing, and hearing one product name but prescribing, transcribing, and dispensing another. There are numerous case reports that describe prescriptions being written correctly, typed correctly, but filled incorrectly on initial fills as well as product refills. Also, physicians have reported of thinking of one drug product but prescribing another. These errors cannot be blamed on incompetence since the same errors are occurring to numerous individuals on a large scale.

3. *Sponsor's Comments:*

As described in the second Med-ERRS Failure Mode and Effects Analysis, there is a low risk of confusion between *[redacted]* and *Glyset* that could lead to medication errors. This report is based on a detailed, side by side comparison of the two products that tracked them from the wholesaler, pharmacy storage, prescribing physician, techniques for prescribing, order entry at the pharmacy, selection of product at pharmacy, dispensing, and finally patient administration. At each step in this eight-step sequence, the report describes a "low risk of confusion", with the exception of pharmacy shortage, where the risk of confusion was described as "moderate". The controlled distribution procedures described above further reduce this moderate risk in practice.

*OPDRA's Comments:*

It is unclear on how the second Med-ERRS evaluation was conducted. No details of the methodology was given, no information on the criteria used to determine whether or not the situation was a low, moderate, or high-risk of confusion, no indication of who determined the levels of confusion and how those levels were determined, and no validation of method was indicated. The evaluation lacks pertinent information and cannot be accurately evaluated by OPDRA.

However, in evaluating the second Med-ERRS analysis, OPDRA has the following comments:

- a) **Storing drug on pharmacy shelf:** Med-ERRS state that there would be three drug products between *[redacted]* and *Glyset* when placed alphabetically on the shelf. The distance between the two products is still relatively close. Even though *[redacted]* is not automatically shipped to the retail pharmacy, a pharmacy will keep it in stock if a patient is on the medication. Please refer to the above comment 1.

b) **Physician type:** The general practice physicians would be at higher risk for mistakenly prescribing [redacted] instead of *Glyset* due to name confusion since they treat a wider population of patients that may include patients with diabetes and/or cancer. The chance of a general practitioner being familiar with both [redacted] and *Glyset* may be higher than an oncologist knowing about both [redacted] and *Glyset* due to the specialty of practice.

c) **How physicians prescribe:** Practitioners may communicate verbally to the patient on how to take the medications while giving the directions on the prescription as "use as directed". Please refer to the above example regarding Celebrex, Celexa, and Cerebyx. As indicated in the first Med-ERRS evaluation, respondents commented that they would pronounce [redacted] with a long "i" if they were not given a pronunciation guide. In reality, not every practitioner and pharmacist will pronounce [redacted] 'glee' vek, but [redacted] with a long "i". The sound-alike similarity would still exist.

According to Webster's New World Dictionary (third college edition), the usual pronunciation of "i" can be found in "is", "hit", and "mirror" and the pronunciation of a long "i" can be found in "ice", "bite", "high", and "sky". Your proposed pronunciation of [redacted] as "Gleevec" is not a normal pronunciation of "i" and this was confirmed in both FDA and Med-ERRS analysis.

d) **Order entry into pharmacy computer:** Different mnemonics is irrelevant when a pharmacist misinterprets or is given the wrong drug name. In a retail setting, the proprietary drug name is usually given instead of the generic name.

e) **Drug administration:** "Physical characteristics of dosage form are very dissimilar, and would be recognized by a patient or caregiver familiar with its use." OPDRA wants to prevent having the wrong drug product get into the patient's hands. A patient or caregiver may not be paying close attention to what is being given, especially when a patient could be taking more than one medication. When the drug is used the first time by the patient or administered the first time by the caregiver, they may not be able to recognize the drug.

#### 4. Sponsor's Comments:

The dose and administration guidelines will also serve to minimize confusion. The usual maintenance dose of *Glyset* is 50 mg 3 times daily, with a maximum recommended dose of 100 mg 3 times daily. [redacted] will be prescribed for chronic phase CML as 400 mg (4 capsules) given once daily, for advance phase CML 600 mg (6 capsules) given once daily.

#### OPDRA's Comments:

The different dosing and administration guidelines do not rule out the possibility of a medication error occurring. Both products can be prescribed as 100 mg, use as directed. As seen in the above Celebrex, Celexa, and Cerebyx example, there was confusion among them even though the dosing and directions are different.

#### 5. Sponsor's Comments:

In the first Med-ERRS evaluation, all 37 pharmacist respondents were given the Novartis pronunciation [redacted] and none of them mentioned *Glyset* as a potential problem with a verbal order. US practitioners did point out that without specific instructions the tendency was to pronounce [redacted] with the long "i" sound, as it would sound with a "gly" prefix. However, based on the second Med-

ERRS Failure Mode and Effects Analysis, we believe the risk is low for creating confusion that would lead to medication errors. To further reduce any potential risk we also plan to include a pronunciation guide in our educational programs.

*OPDRA's Comments:*

The first Med-ERRS report cannot be accurately evaluated by OPDRA due to a lack of important information. Such information include the details on the methodology of the study, the criteria for the selection of the participants, the demographics of the participants, the practice setting of each participant, how the participants were selected (sampling frame), how the prescriptions were distributed, how the prescriptions were given (eg. Was the name given as part of a full prescription as in the real world?), the environment of the study (eg. Did it take place in a busy setting as in the real world?), how the scores were derived and how do the scores relate to actual events. The validation of the techniques used is also not given. The sample size used (37) in the study is quite small; not enough to detect all possible name confusions that might occur when the proprietary is put out in the real world. Also, this study cannot be applied to the review of [redacted] when pronounced with a long "i" and *Glyset* since the study uses the pronunciation as glee' vek. Even comments from the respondents in the sponsor's study stated that they would have pronounced it [redacted] with a long "i". The general population may also pronounce [redacted] with a long "i".

One note, with the pronunciation of glee' vek, but spelled "Glyvek", the study indicated that *Glyset* sounded slightly similar. *Guaivent* was also indicated as sounding similar to [redacted] however, it sounds more like [redacted] instead of [redacted].

According to USAN, the use of "gli" as a prefix in a drug name indicates that the drug is a hypoglycemic agent. Using the name [redacted] would be misleading healthcare practitioners to believing that the drug product is a hypoglycemic agent.

6. *Sponsor's Comments:*

The extensive exchange of information within the media (print & TV) concerning [redacted] over the past four months, and particularly in the most recent period surrounding the publication of our Phase I studies in the New England Journal of Medicine, many health practitioners and CML patients are aware of [redacted] a promising new treatment for the selected indications. This awareness translates to extraordinary name recognition, and this should further reduce the likelihood of prescription-writing or dispensing errors at launch and beyond. Finally, reference is made to over 630 million references made over the last four months surrounding the use [redacted] plus CML patient internet sites which have prominently featured this trademark (e.g. newcmldrug.com).

*OPDRA's Comments:*

Not every healthcare professional will be educated on the actual pronunciation of [redacted] Even existing drugs that have been on the U.S. market for years are mispronounced by healthcare professionals. Just recently, an NBC (Channel 4, Washington D.C.) newscaster on the 11 o'clock evening news pronounced the drug as [redacted] with a long "i". Not everyone will pronounce the name correctly even when there is an extensive exchange of information within the media.

### III. RECOMMENDATIONS:

After review of the information submitted by the sponsor, OPDRA does not recommend the use of the name ( ) since most healthcare professionals will pronounce the drug name with a long "i" ( ) This pronunciation would sound similar to *Glyset*. Also, ( ) uses a USAN prefix, gli-, which indicates that the drug is a hypoglycemic agent. It is against Agency's policy to use a USAN prefix and/or suffix when its meaning is not indicated for that drug product. Using the name ( ) would be misleading healthcare practitioners to believing that the drug product is a hypoglycemic agent.

However, OPDRA recommends the sponsor to revise the spelling of the proprietary name to "Gleevec" so that it is spelled the way it is pronounced. Even though the sponsor's study indicated that *Glyset* and *Guaivent* sound slightly similar to ( ) OPDRA believes that the names sound different enough to reduce the potential risk of confusion. Also, the sponsor's study indicated that *Glucose* looks similar to "Gleevec"; however, glucose tablets are over-the-counter products, which would decrease the potential risk of confusion.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, R.Ph. at 301-827-3231.

/S/ 4/17/01

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Jennifer Fan, Pharm.D.  
Safety Evaluator  
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/ 4/17/01

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Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment

**CONSULTATION RESPONSE**  
**Office of Post-Marketing Drug Risk Assessment**  
**(OPDRA; HFD-400)**

**DATE RECEIVED:** 4/11/01

**DUE DATE:** 4/16/01

**OPDRA CONSULT:** 00-0295

**TO:**

Richard Pazdur, M.D.  
Director, Division of Oncology Drug Products  
HFD-150

**THROUGH:**

Ann Staten  
Project Manager, Division of Oncology Drug Products  
HFD-150

**PRODUCT NAME:**

(Imatinib mesylate) Capsules  
50 mg and 100 mg

**MANUFACTURER:** Novartis Pharmaceuticals Corporation

**NDA #:** 21-335

**SAFETY EVALUATOR:** Jennifer Fan, Pharm.D.

**EXECUTIVE SUMMARY:** In response to a consult from the Division of Oncology Drug Products (HFD-150), OPDRA conducted a review of the proposed proprietary name to determine the potential for confusion with approved proprietary and generic names as well as pending names and did not recommend the use of the proprietary name. OPDRA's review was forwarded to the Division who then forwarded the comments to the sponsor for review and comment. The sponsor responded to our comments with a submission dated April 10, 2001.

**OPDRA RECOMMENDATION:** After review of the information submitted by the sponsor, OPDRA does not recommend the use of the name. However, OPDRA recommends the sponsor to revise the spelling of the proprietary name to "Gleevec" so that it is spelled the way it is intended to be pronounced.

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*S/*

Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment  
Phone: 301-827-3242  
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Martin Himmel, M.D.  
Deputy Director  
Office of Post-Marketing Drug Risk Assessment  
Center for Drug Evaluation and Research  
Food and Drug Administration

HFD-400; Rm. 15B03  
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: March 27, 2001  
NDA NUMBER: 21-335  
NAME OF DRUG: [ (imatinib mesylate) Capsules, 50 mg and 100 mg  
NDA HOLDER: Novartis Pharmaceuticals Corporation

I. INTRODUCTION:

This consult was written in response to a request from the Division of Oncology Drug Products (HFD-150) for assessment of the tradename [ ]

PRODUCT INFORMATION

[ ] is a protein-tyrosine kinase inhibitor. It is indicated for the treatment of patients with chronic myeloid leukemia in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy. [ ] is available in 50 mg and 100 mg hard gelatin capsules.

II. RISK ASSESSMENT:

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts<sup>1,2,3</sup> as well as several FDA databases<sup>4</sup> for existing drug names which sound alike or look alike to [ ] to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>5</sup>. An expert panel discussion was conducted to review all findings from the searches. In addition, OPDRA conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

<sup>1</sup> MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2000).

<sup>2</sup> American Drug Index, 42<sup>nd</sup> Edition, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>4</sup> The Established Evaluation System [EES], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-00, and the electronic online version of the FDA Orange Book.

<sup>5</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

An Expert Panel discussion was held by OPDRA to gather professional opinions on the safety of the proprietary name [redacted] Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

Several product names were identified in the Expert Panel Discussion that were thought to have potential for confusion with [redacted] These products are listed in Table 1, along with the dosage forms available and usual FDA-approved dosage.

Significant concerns were raised in connection with potential confusion between [redacted] and Glyset.

Table 1

Product Name	Dosage form(s), Generic name	Usual adult dose*	Other**
[redacted]	Imatinib Mesylate (Anti-neoplastic - Rx) Capsule: 50 mg and 400 mg	400 mg once a day	[redacted]
Glyset	Miglitol (Anti-diabetic - Rx) Tablet: 25 mg, 50 mg, and 100 mg	50 mg three times a day.	S/A per OPDRA
Lidex	Fluocinonide (Anti-inflammatory - Rx) Ointment, Cream, Solution, Gel: 0.05%	Apply 2 to 4 times a day.	S/A per OPDRA
Videx	Didanosine (ddI) (Anti-retroviral - Rx) Tablet: 25 mg, 50 mg, 100 mg, 150 mg Powder for oral solution, buffered: 100 mg, 167 mg, 250 mg Powder for oral solution, pediatric: 2 g, 4 g	Tablet: If $\geq$ 60 kg, then 400 mg once a day or 200 mg twice a day. If < 60kg, then 250 mg once a day or 125 mg twice a day.	S/A per OPDRA
		*Frequently used, not all-inclusive	**S/A(Sound-alike), L/A (Look-alike)

## B. PRESCRIPTION ANALYSIS STUDIES

### 1. Methodology:

Studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of [redacted] and with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 87 healthcare professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. An OPDRA staff member wrote one inpatient prescription and one outpatient prescription, each consisting of a combination of marketed and unapproved drug products and prescriptions for [redacted] (see below). These written prescriptions were optically scanned and one prescription was delivered via e-mail to each study participant. In addition, one OPDRA staff member recorded a verbal

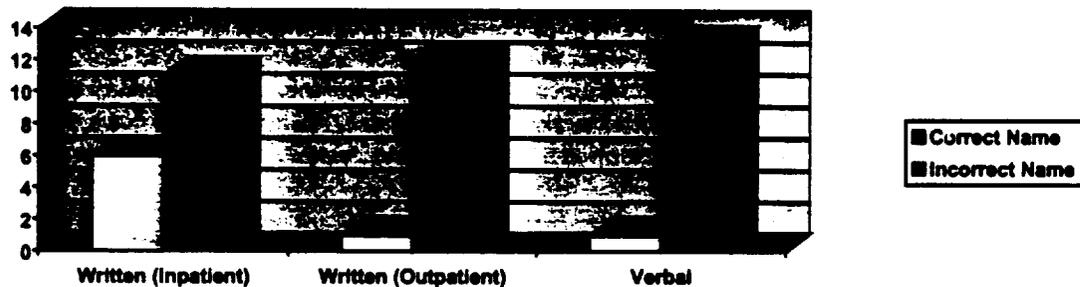
outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via e-mail.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
<p>Inpatient: 400 mg po QD</p> <p>Outpatient: 100 mg Sig: 4 cap qd #120</p>	<p>Outpatient: 100 mg Take 4 capsules daily. #120</p>

2. Results:

Results of these exercises are summarized below:

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written: Inpatient	28	17 (61%)	6 (35%)	11 (65%)
Outpatient	30	13 (43%)	1 (8%)	12 (92%)
Verbal: Outpatient	29	14 (48%)	1 (7%)	13 (93%)
Total	87	44 (51%)	8 (18%)	36 (82%)



Among the verbal outpatient prescriptions, 13 (93%) out of 14 respondents interpreted incorrectly. One participant interpreted the sponsor's proprietary tradename as *Glynase*. Other interpretations include *Glybec*, *Glyvec*, *Glydex*, and *Glyvic*.

Among the written outpatient prescriptions, 12 (92%) out of 13 respondents interpreted incorrectly. Other interpretations include *Glinee*, *Glicus*, *Glivee*, *Gliver*, *Glirce*, *Glince*, *Qlivee*, *Glivu*, *Glinense*, and *Gliurea*.

Among the written inpatient prescriptions, 11 (65%) out of 17 respondents interpreted incorrectly. Interpretations included *Glivac*, *Gilivac*, *Glivia*, and *Glivea*.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name ( ) the primary concerns raised were related to sound-alike, look-alike names that already exist in the U.S. marketplace. Such sound-alike and/or look-alike names include *Videx*, *Lidex*, and *Glyset*.

*Videx* is an anti-retroviral that is indicated for the treatment of HIV-1 infection. *Videx* sounds similar to ( ) Both names contain two syllables and the "idex" and "ivec" in *Videx* and ( ) respectively, sound very similar. Also, like ( ), *Videx* is available in an oral dosage form and is supplied in the 50-mg and 100-mg strength as well as a 25-mg and 150-mg strength. Also, both drug products can be given as 400 mg once a day. However, the sound of the "V" and the "Gl" in *Videx* and ( ) may be different enough that the potential risk of the two proprietary names being confused is decreased.

*Lidex* is a topical, corticosteroid, anti-inflammatory drug product. *Lidex* sounds similar to ( ) The "livec" in ( ) sounds similar to *Lidex*; however, the sound of the "G" in ( ) would distinguish the two names. In the verbal portion of the OPDRA study, one respondent interpreted ( ) as *Glydex*. Also, the dosage forms of the two drug products are different. *Lidex* is available as a topical 0.05% ointment, cream, solution, and gel while ( ) is only available in a capsule form. The directions on the usage of the two drug products are also quite different especially since *Lidex* is a topical medication that is applied 2 to 4 times a day while ( ) is a capsule given once a day. These differences would decrease the potential risk of confusion between the two drug products.

*Glyset* is an anti-diabetic agent and is indicated for the treatment of Type 2 diabetes. *Glyset* and ( ) sound similar. The "Gli" in ( ) and the "Gly" in *Glyset* sound exactly the same when pronounced. In the verbal portion of the study OPDRA conducted for ( ) 13 out of 14 respondents interpreted the "Gli" in ( ) as "Gly". The sound of the "ec" in ( ) can sound like "et" in *Glyset*. Both drug products are available in an oral dosage form and have overlapping strengths (50 mg and 100 mg). Also, *Glyset* is a relatively new drug product on the market; it was approved in December 1996.

However, the difference in the sounds of the "v" and "s" in ( ) and *Glyset*, respectively, may distinguish the two proprietary names. The usual adult dosing schedule on both drug products are different. *Glyset* is given three times a day while ( ) is given once a day. Even with the above mentioned differences, there still is a potential risk of confusion between the two drug products. The directions can be substituted by the prescriber with a "use as directed" direction, thereby, eliminating a distinguishing factor between the two products. Even though *Glyset* is available in tablet form while ( ) is in a capsule form, the dosage form is usually not indicated when the prescription is written. *Celebrex* and *Celexa* has been confused with each other even though *Celebrex* is available in capsule form while *Celexa* is available in tablet form. Like ( ) and *Glyset*, *Celebrex* and *Celexa* can be distinguished by a single sound of a letter, the "b" sound in *Celebrex*. *Celebrex* and *Celexa* do not have overlapping strengths; however, *Celebrex* is available as a 200-mg capsule while *Celexa* is available as a 20-mg tablet. *Celebrex* and *Cerebyx* have also been confused with each other. They both use a different route of administration (oral vs. IV/IM), different dosage form (capsule vs. injection), different directions of use, and a slight difference in the sound of the names. *Celebrex* (December 1998), *Celexa* (oral solution: December 1999, tablet: April 2000), and *Cerebyx* (August 1996) have all been recently approved within close proximity with each other. By comparing *Celebrex*, *Celexa*, and *Cerebyx* to ( ) and *Glyset*, it is possible to see the potential risk of confusion with ( ) and *Glyset*.

If [redacted] was mistakenly given instead of *Glyset*, the patient would be exposed to unnecessary side effects such as neutropenia or thrombocytopenia as well as nausea, vomiting, diarrhea, myalgias, and muscle cramps. Also, the patient would not be receiving *Glyset*, causing the patient's diabetes to be uncontrolled. If *Glyset* was mistakenly given instead of [redacted] the patient's leukemia would not be effectively treated. Also, by taking *Glyset*, the patient would be exposed to unnecessary side effects such as flatulence, diarrhea, and abdominal cramps.

One respondent from the verbal portion of the OPDRA study interpreted [redacted] as *Glynase*. *Glynase* is a sulfonylurea, anti-diabetic drug product. The pronunciation of the first three letters ("Gli" and "Gly") is the same. The endings of both names are different, which might distinguish one drug product from the other. However, as mentioned above, *Celebrex* and *Celexa* were confused even though the endings of their names were different. Like [redacted] *Glynase* can be given once a day. There are no overlapping strengths. *Glynase* is available as a 1.5-mg, 3-mg, and 6-mg tablet while [redacted] is available in 50 mg and 100 mg. *Glynase* has also been on the market since March 1992. It is possible that a prescriber or pharmacist may confuse the two names, especially practicing in a very busy environment. If a patient received *Glynase* instead of [redacted] the patient would be at risk for becoming hypoglycemic, leading into shock, along with the other adverse events associated with the drug product. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretations with these drug products. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

Due to the similarities between [redacted] and *Glyset* and the positive finding in the OPDRA study, OPDRA does not recommend the use of the proprietary name [redacted]

### III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

#### A. CONTAINER LABEL (50 mg and 100 mg; 30, 100, 120, and 180 count bottles)

1. The statement indicating the net quantity of capsules in the bottle should be placed away from the strength of the drug product. For example, the "30 capsules" on the 50-mg strength label should be placed below the "Rx only" statement.
2. The statement "per capsule", which follows the strength of the drug product, should be deleted since it is unnecessary and understood.
3. Since there is more than one strength (50 mg and 100 mg), the strengths should be differentiated between each other. For example, the 50-mg label could be in a different color than the 100 mg label.
4. The statement "Dosage: See package insert" should be revised to state "Usual dosage: See package insert".
5. According to the "How Supplied" section of the package insert, it would seem as though the product contains 50 mg and 100 mg of imatinib. The proposed label states that the product contains 50 or 100 mg of imatinib mesylate. We would recommend that the established name and expression of strength be expressed as the following:

(imatinib)  
Capsules  
50 mg

In addition, the "Description" section of the package insert should clarify the salt as follows:

Each capsule, for oral administration, contains imatinib mesylate equivalent to ... mg of Imatinib. In addition each capsule contains the following inactive ingredients...

#### IV. COMMENTS TO THE SPONSOR

In reviewing the proprietary name ( ), the primary concerns raised were related to sound-alike, look-alike names that already exist in the U.S. marketplace. Such sound-alike and/or look-alike names include *Videx*, *Lidex*, and *Glyset*.

*Videx* is an anti-retroviral that is indicated for the treatment of HIV-1 infection. *Videx* sounds similar to ( ). Both names contain two syllables and the "idex" and "ivec" in *Videx* and ( ) respectively, sound very similar. Also, like ( ) *Videx* is available in an oral dosage form and is supplied in the 50-mg and 100-mg strength as well as a 25-mg and 150-mg strength. Also, both drug products can be given as 400 mg once a day. However, the sound of the "V" and the "G" in *Videx* and ( ) are different enough that the potential risk of the two proprietary names being confused is decreased.

*Lidex* is a topical, corticosteroid, anti-inflammatory drug product. *Lidex* sounds similar to ( ). The "livec" in ( ) sounds similar to *Lidex*; however, the sound of the "G" in ( ) would distinguish the two names. In the verbal portion of the OPDRA study, one respondent interpreted ( ) as *Glydex*. Also, the dosage forms of the two drug products are different. *Lidex* is available as a topical 0.05% ointment, cream, solution, and gel while ( ) is only available in a capsule form. The directions on the usage of the two drug products are also quite different especially since *Lidex* is a topical medication that is applied 2 to 4 times a day while ( ) is a capsule given once a day. These differences would decrease the potential risk of confusion between the two drug products.

*Glyset* is an anti-diabetic agent and is indicated for the treatment of Type 2 diabetes. *Glyset* and ( ) sound similar. The "Gli" in ( ) and the "Gly" in *Glyset* sound exactly the same when pronounced. In the verbal portion of the study OPDRA conducted for ( ) 13 out of 14 respondents interpreted the "Gli" in ( ) as "Gly". The sound of the "ec" in ( ) can sound like "et" in *Glyset*. Both drug products are available in an oral dosage form and have overlapping strengths (50 mg and 100 mg). Also, *Glyset* is a relatively new drug product on the market; it was approved in December 1996.

However, the difference in the sounds of the "v" and "s" in ( ) and *Glyset*, respectively, may distinguish the two proprietary names. The usual adult dosing schedule on both drug products are different. *Glyset* is given three times a day while ( ) is given once a day. Even with the above mentioned differences, there still is a potential risk of confusion between the two drug products. The directions can be substituted by the prescriber with a "use as directed" direction, thereby, eliminating a distinguishing factor between the two products. Even though *Glyset* is available in tablet form while ( ) is in a capsule form, the dosage form is usually not indicated when the prescription is given. *Celebrex* and *Celexa* has been confused with each other even though *Celebrex* is available in capsule form while *Celexa* is available in tablet form. Like ( ) and *Glyset*, *Celebrex* and *Celexa* can be distinguished by a single sound of a letter, the "b" sound in *Celebrex*. *Celebrex* and *Celexa* do not have

overlapping strengths; however, Celebrex is available as a 200-mg capsule while Celexa is available as a 20-mg tablet. Celebrex and Cerebyx have also been confused with each other. They both use a different route of administration (oral vs. IV/IM), different dosage form (capsule vs. injection), different directions of use, and a slight difference in the sound of the names. Celebrex (December 1998), Celexa (oral solution: December 1999, tablet: April 2000), and Cerebyx (August 1996) have all been recently approved within close proximity with each other. By comparing Celebrex, Celexa, and Cerebyx to [redacted] and Glyset, it is possible to see the potential risk of confusion with [redacted] and Glyset.

If [redacted] was mistakenly given instead of Glyset, the patient would be exposed to unnecessary side effects such as neutropenia or thrombocytopenia as well as nausea, vomiting, diarrhea, myalgias, and muscle cramps. Also, the patient would not be receiving Glyset, causing the patient's diabetes to be uncontrolled. If Glyset was mistakenly given instead of [redacted] the patient's leukemia would not be effectively treated. Also, by taking Glyset, the patient would be at risk for becoming hypoglycemic along with the other adverse events associated with the drug product.

One respondent from the verbal portion of the OPDRA study interpreted [redacted] as Glynase. Glynase is a sulfonylurea, anti-diabetic drug product. The pronunciation of the first three letters ("Gli" and "Gly") is the same. The endings of both names are different, which might distinguish one drug product from the other. However, as mentioned above, Celebrex and Celexa were confused even though the endings of their names were different. Like [redacted] Glyset can be given once a day. There are no overlapping strengths. Glynase is available as a 1.5-mg, 3-mg, and 6-mg tablet while [redacted] is available in 50 mg and 100 mg. Glynase has also been on the market since March 1992. It is possible that a prescriber or pharmacist may confuse the two names, especially practicing in a very busy environment. If a patient received Glynase instead of [redacted] the patient would be at risk for becoming hypoglycemic along with the other adverse events associated with the drug product. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretations with these drug products. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

Due to the similarities between [redacted] and Glyset and the positive finding in the OPDRA study, OPDRA does not recommend the use of the proprietary name [redacted].

APPEARS THIS WAY  
ON ORIGINAL

#### V. RECOMMENDATIONS:

OPDRA does not recommend the use of the proprietary name [redacted].

OPDRA recommends the above labeling revisions to encourage the safest possible use of the product.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Jennifer Fan at 301-827-3243.

/S/

3/29/01

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Jennifer Fan, Pharm.D.  
Safety Evaluator  
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/

3/29/01

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Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment

**CONSULTATION RESPONSE**  
**Office of Post-Marketing Drug Risk Assessment**  
**(OPDRA; HFD-400)**

**DATE RECEIVED:** 10/22/00      **DUE DATE:** 3/30/01      **OPDRA CONSULT:** 00-0295

**TO:**

Richard Pazdur, M.D.  
Director, Division of Oncology Drug Products  
HFD-150

**THROUGH:**

Ann Staten  
Project Manager, Division of Oncology Drug Products  
HFD-150

**PRODUCT NAME:**

(Imatinib mesylate) Capsules  
50 mg and 100mg

NDA #: 21-335

**MANUFACTURER:** Novartis Pharmaceuticals Corporation

**SAFETY EVALUATOR:** Jennifer Fan, Pharm.D.

**SUMMARY:** In response to a consult from the Division of Oncology Drug Products (HFD-150), OPDRA conducted a review of the proposed proprietary name [redacted] to determine the potential for confusion with approved proprietary and generic names as well as pending names.

**OPDRA RECOMMENDATION:**

OPDRA does not recommend the use of the proprietary name [redacted]

/S/

Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment  
Phone: 301-827-3242  
Fax: 301-480-8173

/S/

Martin Himmel, M.D.  
Deputy Director  
Office of Post-Marketing Drug Risk Assessment  
Center for Drug Evaluation and Research  
Food and Drug Administration

**APPEARS THIS WAY  
ON ORIGINAL**

**MEETING MINUTES**

**MEETING DATE:** August 18, 2000 **TIME:** 1pm **LOCATION:** Conference Room B

**IND/NDA - IND** } Meeting Request Submission Date: June 22, 2000 (N081)  
Briefing Document Submission Date: July 20, 2000 (N086)

**DRUG:** STI571

**SPONSOR/APPLICANT:** Novartis

**TYPE of MEETING:**

1. **pre-NDA - CMC**
2. **Proposed Indication:** Treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia in myeloid blast crisis, accelerated phase, chronic phase (interferon failures).

**FDA PARTICIPANTS:**

John Simmons, Ph.D., Director, Division of New Drug Chemistry I  
Rebecca Wood, Ph.D., Chemistry Team Leader  
Sung Kim, Ph.D., Chemistry Reviewer

**INDUSTRY PARTICIPANTS:**

Morten Bugge Garn, Drug Regulatory Affairs/CMC  
Joerg Ogorka, Technical Research and Development  
Peter Wirz, Technical Research and Development  
Leslie-Martin-Hischak, Drug Regulatory Affairs/CMC

**MEETING OBJECTIVES:**

1. To discuss CMC issues for the NDA submission.

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pages of trade

secret and/or

confidential

commercial

information