CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-068

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mailstop 4447)

DATE RECEIVED: December 20, 2006	**DESIRED COMPLETION DATE:** June 1, 2007	**OSE REVIEW #:** 06-0127 and 2006-1126
DATE OF DOCUMENT: September 29, 2006	**PDUFA DATE:** July 29, 2007	

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HFD-150

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FROM: Todd Bridges, RPh, Safety Evaluator
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PRODUCT NAME: **Tasigna** (Nilotinib Capsules) 200 mg **NDA #:** 22-068 (**IND #:** 69,764)	**SPONSOR:** Novartis

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Tasigna, from a safety perspective. This name evaluation is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review in order to minimize potential errors with the use of this product.

3. DDMAC finds the proposed proprietary name, Tasigna, acceptable from a promotional perspective.

DMETS 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 Samuel Chan, OSE Project Manager, at 301-796-2283.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
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Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: January 4, 2007

NDA #: 22-068 (**IND #:** 69,764)

NAME OF DRUG: **Tasigna**
(Nilotinib Capsules)
200 mg

IND HOLDER: Novartis

I. INTRODUCTION:

This consult was written in response to a request from the Division of Drug Oncology Products (HFD-150), for assessment of the proprietary name, Tasigna, regarding potential name confusion with other proprietary or established drug names. Additionally, the sponsor submitted an independent name analysis [redacted] for review and comment. Container labels, carton and insert labeling were submitted for review and comment.

PRODUCT INFORMATION

Tasigna (Nilotinib) is being developed for the treatment of chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia (CML) in adult patients intolerant to or resistant to [redacted] prior therapy. The recommended dosage regimen is two 200 mg capsules twice daily. Tasigna will be available as 200 mg capsules in weekly packs (28 capsules) [redacted]

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Tasigna to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version

[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)

of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The SAEGIS[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS 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 (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Tasigna. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and 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.

1. DDMAC finds the proposed proprietary name, Tasigna, acceptable from a promotional perspective.

2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Tasigna. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1. Potential Sound-Alike/Look-Alike Names Identified for Tasigna.

Product Name	**Dosage form(s), Established name**	**Usual adult dose***	**Other****
Tasigna	Nilotinib Capsules 200 mg	400 mg (2 capsules) twice daily.	N/A
Tarceva	Erlotinib Tablets 25 mg, 100 mg and 150 mg	Nonsmall cell lung cancer (NSCLC): 150 mg once daily taken at least 1 hour before or 2 hours after the ingestion of food. Pancreatic cancer: 100 mg once daily taken at least 1 hour before or 2 hours after the ingestion of food.	LA/SA
Tussigon	Hydrocodone Bitartrate and Homatropine Tablets 5 mg/1.5 mg	1 tablet every four to six hours.	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

[5] www location http://www.uspto.gov/tmdb/index.html.

[6] Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Tasigna with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. Each study employed a total of 119 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Tasigna (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 	Tasigna 400 mg Quantity 180 1 tablet twice a day
Inpatient RX: [redacted]	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A (page 12) for the complete listing of interpretations from the verbal and written studies.

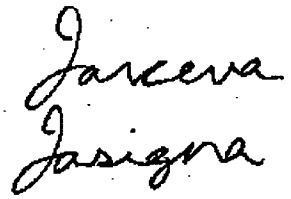
C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proposed proprietary name, the primary concerns relating to look-alike and/or sound-alike confusion with Tasigna are Tarceva and Tussigon.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Tasigna.

1. Tarceva was identified as having look and sound-alike similarities to the proposed name, Tasigna. Tarceva is indicated as monotherapy for the treatment of patients with locally advanced or metastatic Non-small Cell Lung Cancer (NSCLC) after failure of at least one prior chemotherapy regimen. Tarceva is also indicated in combination with gemcitabine for the first-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer. Tarceva is available in 25 mg, 100 mg, and 150 mg tablets. The usual dose for NSCLC and pancreatic cancer is 150 mg and 100 mg, respectively.

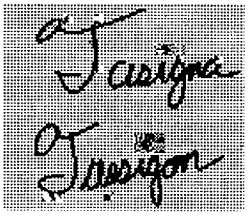
   Both names contain three syllables, begin with the letters "Ta", and have similar endings ("va" vs. "na") which contributes to the phonetic similarities between the two drug names. However, the different sound of the second syllable of each name ("cev" vs. "sig") should serve to distinguish the two names in speech. Look-alike properties between Tarceva and Tasigna stem from the fact that both names begin with the letters "Ta", end with the letter "a", and contain the same number of letters (seven). Additionally, the letter "v" in Tarceva may look like the letter "n" of Tasigna, or vice versa, when scripted (see below). However, the middle letters of each name ("rce" vs. "sig") may help to differentiate this name pair orthographically.



   These two products share the same route of administration (oral). However, Tarceva is supplied in multiple strengths (25 mg, 100 mg, and 150 mg) and thus, on a prescription for Tarceva, the strength will be indicated which will help to differentiate the two drug names. Additionally, Tarceva and Tasigna differ in dose (one tablet vs. two capsules), and frequency of administration (once daily vs. twice daily). Therefore, the dose and frequency of administration indicated on an order may lessen any confusion stemming from similarities involving this name pair. Although Tarceva and Tasigna share some look and sound-alike similarities, the differences in product strength, dose, and frequency of administration will help decrease the potential for confusion and error between these two products.

2. Tussigon may look similar to Tasigna when scripted. Tussigon is a narcotic antitussive indicated for the symptomatic relief of cough. Tussigon is available in 5 mg/1.5 mg (Hydrocodone Bitartrate/Homatropine) tablets. The usual dose is one tablet every four to six hours as needed.

The look-alike similarity stems from the fact both names begin the letter "T" which is followed by letters which can look similar when scripted ("u" vs. "a"). Additionally, each of theses names contain the same combination of letters ("sig") in similar positions. However, the ending letters are different ("na" vs. "on") which may help to distinguish the names from one another on an order (see below).



Additionally Tussigon and Tasigna have non-overlapping product characteristics such as product strength (5 mg/1.5 mg vs. 200 mg), dose (1 tablet vs. 2 capsules), and frequency of administration (every 4 to 6 hours as needed vs. twice daily). Although these products differ in strength, the strength may be omitted on an order since both are only available in one strength. The dose and frequency of administration indicated on an order may lessen any confusion stemming from similarities involving this name pair. Although orthographic similarities exist between Tussigon and Tasigna, DMETS believes the dose and frequency of administration will help to minimize confusion between theses two products.

D. INDEPENDENT NAME ANALYSIS [redacted]

The sponsor employed [redacted] to conduct an independent analysis of the proposed proprietary name, Tasigna. [redacted] determined that overall the proposed trademark, Tasigna, has low vulnerability for look-alike and sound-alike confusion. The specific results of the independent analysis, the Tasigna Trademark Safety Evaluation, are described below:

1. Table I—Look-alike names with potential for confusion

[redacted] did not identify any names that were mentioned by respondents and evaluated [redacted] staff as having the potential for look-alike confusion when handwritten.

DMETS Response

DMETS identified the names Tarceva and Tussigon as having the potential for look-alike confusion when handwritten, however, we feel that product differences (e.g., strength, formulation, dose, and frequency of administration) will help minimize the potential for confusion (See Section IIC).

2. Table II—Sound-alike names with potential for confusion

[redacted] did not identify any names that were mentioned by respondents and evaluated by [redacted] staff as having potential for sound-alike confusion.

DMETS response:

DMETS identified the name Tarceva has the potential for sound-alike confusion with Tasigna (See Section IIC).

3. Table III—Medical terms with potential for confusion

[redacted] did not identify any important medical terms or abbreviations mentioned by respondents as having the potential for look-alike or sound-alike confusion with Tasigna.

DMETS Response:

DMETS acknowledges the findings for Tasigna.

4. Table IV—Respondents' suitability comments (rating) of proposed trademarks

[redacted] identified the following comment from respondent(s): "Reminds one of lasagna".

DMETS response:

DMETS acknowledges the comments regarding the suitability of the name Tasigna. However, it has no bearing on potential sound-alike or look-alike names in the context of prescription or over-the-counter medications.

5. Table V—FDA and USAN Regulatory Assessment

[redacted] presented evaluation criteria drawn from the paper "Avoiding Trademark Trouble at FDA", which was published in the June 1996 issue of *Pharmaceutical Executive.*

DMETS Response:

DMETS cannot comment on the regulatory assessment provided by [redacted] The paper quoted was published in June 1996 and is not currently used by DMETS to evaluate tradenames.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the labels and labeling of Tasigna, DMETS has focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, in the interest of minimizing user error and maximizing patient safety.

A. GENERAL COMMENTS

1. Ensure that the established name is at least one-half the size of the proprietary name in accordance with 21 CFR 201.10(g)(2). Additionally, revise so that the statement of dosage form ("capsules") follows the established name [e.g., (Nilotinib Capsules)].

2. As currently presented, the product strength statement is not in close proximity to the proprietary/established name. Relocate the product strength statement (200 mg) so that it appears juxtaposition to the proprietary and established names. Delete the "per capsule" statement which follows the current product strength. Additionally, increase the font size of the product strength commensurate with the proprietary and established name.

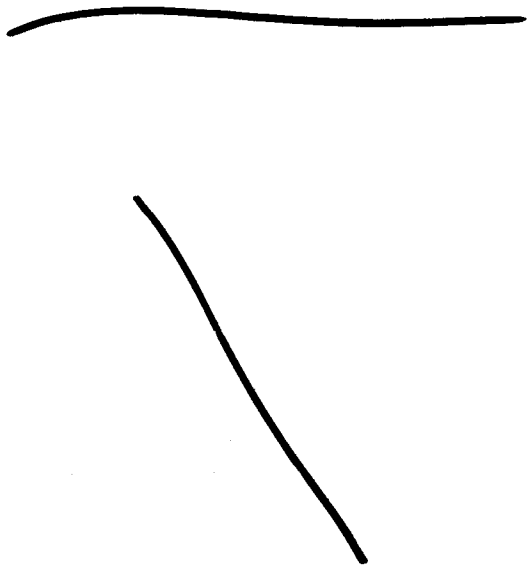
3. Delete the statement "1 capsule contains 200 mg nilotinib" as it is redundant to the product strength statement "200 mg".

4. Increase the prominence of the "Rx Only" statement.

5. Increase the prominence of the "Physicians Sample(s) - Not For Sale" statement.

B. CONTAINER LABEL

1.



c.

d. [redacted]

2. Blister Unit-Dose

   a. See GENERAL COMMENTS A1 through A4.

   b. We recommend adding dosing instructions to the blister card to clearly indicate how to properly take nilotinib.

   c. DMETS recommends using "Day 1", Day 2", etc., as column headings instead of the days of the week since patients beginning therapy with nilotinib on any day other than Sunday may be confused by the day of the week designations.

      Additionally, delete the sun and moon graphics since these may be confusing as well. DMETS recommends using the words "Morning" and "Evening" instead. The terms "Morning" and "Evening" convey more information to the patient than the sun and moon graphics. We recommend the following presentation:

	Day 1 Morning	Day 1 Evening	Day 2 Morning	Day 2 Evening	Day 3 Morning	Day 3 Evening	
add dosing instructions here	O	O	O	O	O	O	
	O	O	O	O	O	O	etc.

   d. Revise the statement of strength to read "200 mg **per capsule"** in order to prevent patients from ingesting the wrong dose (i.e., entire contents of the blister card, less than one capsule, or more than one capsule). See Figure 2 below.

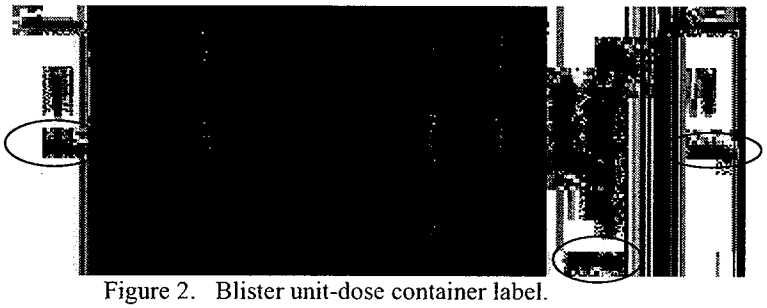


Figure 2. Blister unit-dose container label.

C. CARTON LABELING

1. Individual Folding Carton

   a. Professional Sample

      1. See GENERAL COMMENTS A1 through A5.

      2. To improve the flow and comprehension of the "INSTRUCTIONS FOR USE", delete the purple boxing [i.e., PATIENT STARTER KIT] indicated by the arrow in Figure 3 below. The current presentation cuts off the flow of the instructions and it appears to be a separate set of instructions for a different step instead of a continuation of the previous instructions. Additionally, revise instruction "1." of "Opening Instructions" to include the phrase "(see below)" following the words "button" and "tab".

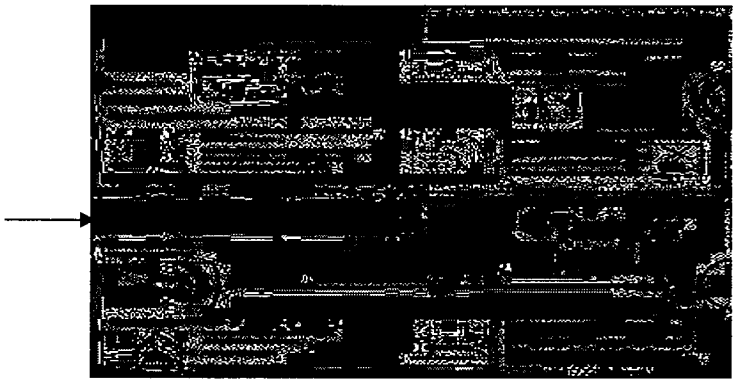


Figure 3. Individual folding carton labeling for professional sample.

      3. Include the statement of product strength wherever the proprietary and established names are presented. The strength should be presented in juxtaposition to the proprietary and established names.

   b. Trade

      See GENERAL COMMENTS A1 through A4 and comments C1a2 and C1a4.

2. Display Carton

   a. Physician Sample

      See GENERAL COMMENTS A1 through A5.

   b. Trade

      See GENERAL COMMENTS A1 through A4.

D. INSERT LABELING

1. The first presentation of the proprietary name in the insert should be accompanied by the established name and product strength. Revise accordingly.

2. 11 DESCRIPTION

   Delete the statement [redacted] since it does not convey any useful information. The container label and carton labeling will contain the actual expiration date which is more useful to patients and health care practitioners.

3. 16 HOW SUPPLIED/STORAGE AND HANDLING

   Include in this section a detailed description of the two packaging configurations which will be available for this product. Additionally, include applicable storage and handling information. See the fictitious example below.

16 HOW SUPPLIED/STORAGE AND HANDLING

The light blue 50 mg capsules with 50 imprinted in dark blue on one side and Indicus on the other are available in unit of use HDPE bottles of:

- **30 capsules (NDC XXXX-XXXX-XX)**
- **60 capsules (NDC XXX-XXXX-XX)**
- **500 capsules (NDC XXX-XXX-XX)**

Storage:

Store at 25° C (77° F); excursions permitted to 15° - 30° C (59° - 86° F) [See USP Controlled Room Temperature.]

Appendix A. Tasigna Prescription Study Results

Inpatient	Outpatient	Voice
Insigna (Fersigna?)	Tasigna	Tasigna
Lasigna	Tarsigna	Tescigna
Lasigna	Tasigna	Tesigna
Tasiegna	Tasigna	Tesigna
Tasigma	Tasigna	Tesigna
Tasigna	Tasigna	Tesigna
Tasigna	Tasigna	Tesigna
Tasigna	Tasigna	tesigna
Tasigna	Tasigna	Tessigna
Tasigna	Tasigna	Testigma
Tasigna	Tasigna	Testigna
Tasigna	Tasigna	Testigna
Tasigna	Tasigna	
Tasiyna	Tasigna	
	Tasigna	
	Tasigna	
	Tasigna	
	Tasigna	
	Tasigna	
	Tasigra	

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/s/

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