CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-861s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	March 6, 2008
To:	Badrul Chowdhury, MD, Director Division of Pulmonary and Allergy Products
Thru:	Kellie Taylor, PharmD, MPH, Team Leader Carol Holquist, RPh, Director Division of Medication Error and Technical Support
From:	Judy Park, PharmD, Safety Evaluator Division of Medication Error Prevention
Subject:	Proprietary Name and Labeling Review
Drug Name(s):	Patanase (Olopatadine Hydrochloride) Nasal Spray) 665 mcg/spray
Application Type/Number:	NDA 21-861
Applicant/applicant:	Alcon
OSE RCM #:	2007-2393

CONTENTS

EXECUTIVE SUMMARY

The Proprietary Name Risk Assessment found that the proposed name, Patanase, has some similarity to other proprietary and established drug names, but the FMEA findings indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention has no objections to the use of the proprietary name, Patanase, for this product.

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling appear to be vulnerable to confusion that could lead to medication errors. The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

However; if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

1.1 INTRODUCTION

This consult was written in response to a request from the Division of Pulmonary and Allergy Products to evaluate the proprietary name, Patanase, and insert labeling to identify areas that could lead to medication errors.

1.2 REGULATORY HISTORY

the Division of Medication Error Prevention reviewed the proprietary name, Patanase, in OSE review #03-0091 and 03-0091-1 dated
August 12, 2005 and had no objection to the name. We re-evaluated the name based on Citizen's Petition dated October 7, 2005 in OSE review #03-0091-2 dated December 1, 2005 and still had no objection to the name.

1.3 PRODUCT INFORMATION

Patanase (Olopatadine Hydrochloride) Nasal Spray is indicated for the management and treatment of the symptoms associated with seasonal allergic rhinitis in patients 12 years of age and older. Each metered spray (100 mL) delivers 665 micrograms of olopatadine hydrochloride, equivalent to 600 mcg of olopatadine base. Patanase will be supplied in a 30.5 gram metered-dose manual spray pump that contains 240 sprays. The recommended dose is two sprays in each nostril twice daily.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error Prevention medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and labeling risk assessment (see 2.2 Container Label, Carton Labeling, and Insert Label Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. THE DIVISION OF MEDICATION ERROR PREVENTION defines a medication error as any preventable event that may

cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Patanase, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Patanase, the medication error staff of the Division of Medication Error Prevention search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and hold a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division of Medication Error Prevention also conducts internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see detail 2.1.4).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the Staff consider the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, the Division of Medication Error Prevention considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[3]

---

[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

[2] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'P' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[45] Also, consideration was given to alternative phonetic pronunciations of the proposed name.

To identify drug names that may look similar to Patanase, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (8 letters), upstrokes (2, capital letter 'P' and 't'), downstokes (none), cross-strokes (1, 't'), and dotted letters (none). Additionally, several letters in Patanase may be vulnerable to ambiguity when scripted, including the letter 'P' may appear as 'B'; lower case 'a' appear as a lower case 'o' or 'e'; lower case 'n' appear as a lower case 'm'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Patanase.

When searching to identify potential names that may look or sound similar to Patanase, the Medication Error Staff search for names with similar number of syllables (3), stresses (pat-UH-nase or PAT-uh-nase), and placement of vowel and consonant sounds. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Patanase), the established name (Olopatadine Hydrochloride), proposed indication (allergic rhinitis), strength (665 mcg), dose (2 sprays in each nostril), frequency of administration (twice daily), route (intranasal) and dosage form of the product (nasal spray). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Data base and information sources

The proposed proprietary name, Patanase, was provided to the medication error staff of the Division of Medication Error Prevention to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Patanase using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names.

---

[4] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[5] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence in Medicine (2005)

The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, Patanase. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Error Prevention. The Medication Error Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.2 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Patanase convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Patanase to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably

[6] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Division of Medication Error Prevention identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug another drug product.

In the event that the Division of Medication Error Prevention objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, the Division of Medication Error Prevention will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while the Division of Medication Error Prevention will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the Division of Medication Error Prevention will not object to the use of the proprietary name. If any of these conditions are met, then the Division of Medication Error Prevention will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Division of Medication Error Prevention contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, the Division of Medication Error Prevention believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If the Division of Medication Error Prevention objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. The Division of Medication Error Prevention is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for the Division of Medication Error Prevention to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so the Division of Medication Error Prevention may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.[7]

Because the Division of Medication Error Prevention staff analyze reported misuse of drugs, the Division of Medication Error Prevention staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. The Division of Medication Error Prevention uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Applicant submitted on September 21, 2007 the following insert labeling for the Division of Medication Error Prevention review (see Appendix C, D, E for images):

- Sample and Retail Container
- Sample and Retail Carton
- Patient's Instructions for Use
- Prescribing Information (no image)

[7] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p. 275.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Data base and information sources

The Division of Medication Error Prevention conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Patanase to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, seven names were identified as having some similarity to the name Patanase.

Five of the seven names that were thought to look like Patanase, which include: Panacet, Betanate, Parnate, Potassium, and (b) (4) Two additional names (b) (4) and Pataday) were thought to look and sound similar to Patanase.

3.1.2 Expert panel discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention staff (see section 3.1.1. above), and noted no additional names thought to have orthographic similarity to Patanase and have the potential for confusion.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.1.3 Safety evaluator risk assessment

Independent searches by the primary Safety Evaluator identified no additional names thought to look similar to Patanase and represent a potential source of drug name confusion.

This analysis determined that the name similarity between Patanase and the identified names was unlikely to result in medication errors for two products. One product (b) (4)) was already reviewed in the previous OSE Review #03-0091-2. (b) (4) was a name the Division of Medication Error Prevention previously objected to for a currently marketed product, Pataday (OSE Review #01-0230-3).

For the remainder of the 5 names identified (Panacet, Betanate, Potassium, Pataday, and Parnate), FMEA determined that medication errors were unlikely because the products do not overlap in strength or dosage with Patanase and have minimal orthographic and/or phonetic similarity to Patanase (Appendix B).

3.2 LABEL AND LABELING RISK ASSESSMENT

A review of the carton and container labels identified several potential sources of medication error, specifically with respect to the graphics and color on the packaging and the presentation of the company name and the established name of the product.

The proposed container and carton labels contain blue dotted graphic above the letter “t” in the proprietary name. There is also prominent graphics of a nasal spray with mist on the principal display panel of the carton label. Some pertinent information is written in dark blue font against the blue background on top of the container and carton labels. Additionally, the size of the company name “Alcon” is just as big as the proprietary name especially on the container labels.

*** Note: This is proprietary and confidential information that should not be released to the public.

The established name is not at least ½ the size of the proprietary name per 21 CFR 201.10(g)(2). Additionally, the established name is presented in its salt form (hydrochloride) and the insert labeling does not include the conversion from the salt to active moiety. The dosage form is located above the proprietary name instead of following the established name. The route of administration is missing or cannot be read against the blue background.

4 DISCUSSION

4.1 PROPRIETARY NAME

The results of the Proprietary Name Risk Assessment found that the proposed name, Patanase, has some similarity to other proprietary and established drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, the Division of Medication Error Prevention believes that these limitations are sufficiently minimized by the use of an Expert Panel, the CDER Prescription Studies that involved 123 CDER practitioners, and, in this case, the data submitted by the Applicant from an independent proprietary name risk assessment firm, which included the responses of frontline practitioners.

4.2 LABEL AND LABELING

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling appears to be vulnerable to confusion that could lead to medication errors.

The Division of Medication Error Prevention is concerned with the graphics (blue dots) above the letter "t" in the proprietary name. This graphic is distracting and interferes with the readability of the proprietary name since the letter "t" can be mistaken for "i" due to the blue dots. Also, the prominent graphic of the spray canister on the principal display panel of the carton label is more prominent than the drug name. The blue background on top third of the label also makes it difficult to read the important information written in dark blue font.

Additionally on the container label, we are concerned of the prominence of the company name. Since the container label will be wrapped around the circular packaging, the prominence of the company name will compete with the prominence of the drug name.

The established name should be at least ½ size of the proprietary name in its font length and width per 21 CFR 201.10(g)(2). However, as proposed, established name appears smaller. We also noticed that the established name is presented in its salt form on the carton labels, which requires clarification from the CDER Labeling and Nomenclature Committee to determine if this is the proper designation. Additionally, the dosage form (i.e. nasal spray) is located on top of the tradename instead of following the established name which is the proper presentation of the established name. Lastly, the route of administration which is required per 21 CFR 201.100(b)(3) is missing on the labels.

5 CONCLUSIONS AND RECOMMENDATION

The Proprietary Name Risk Assessment findings indicate that the proposed name, Patanase, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention does not object to the use of the proprietary name, Patanase, for this product.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed carton and container labels introduces vulnerability to confusion that could lead to medication errors. The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

5.1 COMMENTS TO THE DIVISION

The Division of Medication Error Prevention has no objections to the use of the proprietary name, Patanase, for this product. However, if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

Based upon our assessment of the proprietary name, labels and labeling, the Division of Medication Error Prevention has identified areas needed of improvement. We have provided recommendations in Section 5.2 and request this information be forwarded to the Applicant. The Division of Medication Error Prevention also recommends that the Division consult Richard Lostritto, Chair of the CDER Labeling and Nomenclature Committee (LNC) and the assigned ONDQA Chemist for further assistance regarding the proper designation of the established name and strength.

The Division of Medication Error Prevention would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention on any communication to the applicant with regard to this review. If you have further questions or need clarifications, please contact Anne Crandall, project manager, at 301-796-2282.

5.2 COMMENTS TO THE APPLICANT

The Division of Medication Error Prevention has no objections to the use of the proprietary name, Patanase, for this product. Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Applicant to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

However, our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the Division of Medication Error Prevention

recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

5.2.1 Proprietary Name:

1. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review.

5.2.2 Labels and Labeling:

5.2.2.1 General Comments

1. The established name should be presented in the active moiety form and the dosage form (i.e. nasal spray) should follow the established name. Therefore, the established name should be presented as "Olopatadine Nasal Spray 600 mcg." Additionally, be consistent in the presentation of the established name and strength throughout the labeling.

5.2.2.2 Container Labels

1. Decrease the prominence of the company name on the container label so that it does not compete with the prominence of the drug name.
2. Remove the graphics (i.e. blue dots) above the letter "t" in the proprietary name.
3. Increase the size of the established name so that it is at least ½ size of the proprietary name in its font length and width per 21 CFR 201.10(g)(2).
4. The Division of Medication Error Prevention recommends including the route of administration (i.e. For Intranasal Use Only) per 21 CFR 201.100(b)(3).
5. Change the font color of the information written against the blue background of the top third of the carton label or change the blue background so that the information can be easily read.

5.2.2.3 Carton Labeling

1. Decrease the prominence of the main graphics (i.e. nasal spray with mist) and relocate it away from the principal display panel so that it does not compete with the prominence of the drug name.
2. Remove the graphics (i.e. blue dots) above the letter "t" in the proprietary name.
3. Increase the size of the established name so that it is at least ½ size of the proprietary name in its font length and width per 21 CFR 201.10(g)(2).
4. The Division of Medication Error Prevention recommends including the route of administration (i.e. For Intranasal Use Only) per 21 CFR 201.100(b)(3).
5. Change the font color of the information written against the blue background of the top third of the carton label or change the blue background so that the information can be easily read.

6 REFERENCES

6.1 PREVIOUS REVIEWS

1. OSE Review #03-0091 and 03-0091-1, Proprietary Name Review of Patanase, Culley, K.; August 12, 2005.

2. OSE Review #03-0091-2, Proprietary Name Review of Patanase, Culley, K.; December 1, 2005.

6.2 DATABASES

1. Micromedex Integrated Index (http://weblern/)

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for THE DIVISION OF MEDICATION ERROR PREVENTION , FDA.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://weblern/)

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

5. Division of Medication Errors and Technical Support proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention from the Access database/tracking system.

6. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

7. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. WWW location http://www.uspto.gov.

Provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (http://weblern/)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (http://weblern/)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Stat!Ref (http://weblern/)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.pharmacist.com)

A web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Division of Medication Error Prevention also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the Division of Medication Error Prevention will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, the Division of Medication Error Prevention also considers a variety of pronunciations that could occur in the English language.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstokes Downstrokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Products with no numerical overlap in strength and dose.

Patanase (Olopatadine Hydrochloride)		**665 mcg/spray**	**2 sprays per nostril twice daily**
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Panacet	Sound	5 mg/500 mg	1-2 tablets every 4-6 hours
Betanate	Look	0.05 %	Apply to affected area daily
Potassium	Look	Varies	Prevention: 16-24 mEq/day Treatment: 40-100 mEq/day
Parnate	Look	10 mg	30 mg/day in divided dose
Pataday	Look/Sound	0.2 %	1 drop in each affected eye daily

2 pp withheld immed after this page as (b)(4) draft labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Kellie Taylor
3/6/2008 03:56:42 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/6/2008 04:06:07 PM
DRUG SAFETY OFFICE REVIEWER

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; White Oak 22, Mail Stop 4447)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**ODS CONSULT #:**
November 27, 2005	December 1, 2005	03-0091-2
DOCUMENT DATE:	**PDUFA DATE:**	
October 5, 2005	October 7, 2005	

TO: Badrul Chowdhury, MD
Director, Division of Pulmonary and Allergy Products
HFD-570

THROUGH: Anthony Zeccola
Project Manager, Division of Pulmonary and Allergy Products
HFD-570

FROM: Kimberly Pedersen, RPh, Safety Evaluator
Alina Mahmud, RPh, MS, Team Leader

PRODUCT NAME: **Patanase** (Olopatadine Hydrochloride) Nasal Spray 665 mcg/spray **NDA#: 21-861**	**NDA SPONSOR:** Alcon Research

RECOMMENDATIONS:

After a review of the names submitted in the Citizen's Petition, DMETS continues to have no objections to the use of the proprietary name, Patanase (see Section III for details).

Denise Toyer, PharmD Deputy Director Division of Medication Errors and Technical Support Office of Drug Safety	Carol Holquist, RPh Director Division of Medication Errors and Technical Support Office of Drug Safety Phone: (301) 796-2360 Fax: (301) 796-9865

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; White Oak 22, Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: November 23, 2005

NDA# 21-861

NAME OF DRUG: **Patanase** (Olopatadine Hydrochloride) Nasal Spray
665 mcg/spray

NDA HOLDER: **Alcon Research**

I. INTRODUCTION:

This consult was written in response to a Citizen's Petition concerning the proposed tradename Patanase with the resultant consult request from the Division of Pulmonary and Allergy Products (HFD-570) for a re-assessment of the proprietary name Patanase in regard to the names listed in the citizen's petition that may result in potential name confusion.

PRODUCT INFORMATION

Patanase (Olopatadine Hydrochloride) Nasal Spray is indicated for the (b) (4) treatment of the symptoms associated with seasonal (b) (4) allergic rhinitis in patients 12 years of age and older. Each metered spray delivers 665 micrograms of olopatadine, equivalent to 600 mcg of olopatadine base. Patanase will be supplied in a 30.5 gram metered-dose manual spray pump that contains 240 sprays. The recommended dose is two sprays in each nostril twice daily.

II. RISK ASSESSMENT:

(b) (4) identified nine names in their Citizen's Petition that were thought to have the potential for confusion with Patanase. These products with the available dosage forms and usual dosage are listed in table 1 (see below and page 3).

Table 1: Potential Sound-Alike/Look-Alike Names Identified by the Citizen's Petition

Product Name	Established name, Dosage Form(s), Strength(s)	Usual adult dose*	Other**
Patanase	Olopatadine HCl Nasal Spray 665 mcg per spray	2 sprays in each nostril twice daily	
Panokase Panokase 16	Amylase/Lipase/Protease Tablets, 30,000 Units/8,000 units/30,000 units 60,000 Units/16,000 units/60,000 Units	Cystic fibrosis and chronic pancreatitis patients: Dose ranges from 8,000 to 32,000 lipase units (1 to 4 tablets with meals). Pancreatectomy or obstruction of pancreatic ducts: 1 to 2 tablets every 2 hours.	

Table 1: Potential Sound-Alike/Look-Alike Names Identified by the Citizen's Petition			
Product Name	Established name, Dosage Form(s), Strength(s)	Usual adult dose*	Other**
Patanase	Olopatadine HCl Nasal Spray 665 mcg per spray	2 sprays in each nostril twice daily	
Pancrease® Pancrease® MT 4 Pancrease® MT 10 Pancrease® MT 16 Pancrease® MT 20	Amylase/Lipase/Protease Delayed Release Capsule, 20,000 Units, 4,500 Units, 25,000 Units 12,000 Units, 4,000 Units, 12,000 Units 30,000 Units, 10,000 Units, 30,000 Units 48,000 Units, 16,000 Units, 48,000 Units 56,000 Units, 20,000 Units, 44,000 Units	Infants (up to 12 months): 2,000 to 4,000 lipase units per 120 mL of formula or breast milk. Under 4 years of age: Start with 1,000 lipase units/kg/meal up to a maximum of 2,500 lipase units/kg/meal. Over 4 years of age: Start with 400 lipase units/kg/meal up to a maximum of 2,500 lipase units/kg/meal.	LA/SA
Panase	Pancreatin, Pancrelipase		LA/SA
Paltrase	Pancrelipase		LA/SA
Palipase	Pancrelipase		LA/SA
Protilase	Pancrelipase		LA/SA
Papase	Papain		LA/SA
Pentasa®	Mesalamine Controlled Release Capsules, 250 mg and 500 mg	1 gram four times daily, used for a duration of 8 weeks in clinical trials	LA/SA
Pannaz® Pannaz S	Carbinoxamine Maleate/Methscopolamine Nitrate/Pseudoephedrine Hydrochloride Extended Release Tablet 8 mg, 2.5 mg, 90 mg Carbinoxamine maleate/Methscopolamine Nitrate/Pseudoephedrine Hydrochloride Syrup 2 mg, 1.25 mg, 15 mg	1 every 12 h up to 2/day 5 to 10 mL 4 times a day	LA/SA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

Upon searching for information on the above referenced drug product names identified in the citizen's petition, it appears only four products (Panokase, Pancrease, Pentasa, and Pannaz) are currently marketed in the United States.

The drug names of Panase, Paltrase, Palipase, Protilase and Papase do not appear in US drug references such as Red Book, Facts and Comparisons, and Clinical Pharmacology. A review of Martindale's, a compendium of foreign drug names lists the following:

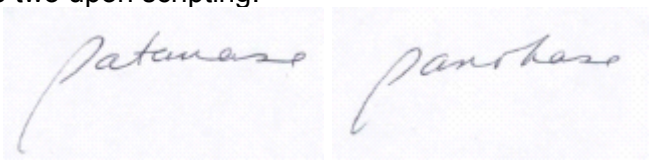
- Panase as "Pancreatin" and "Pancrelipase", but no reference to the drug being marketed anywhere in the world.
- Paltrase as Paltrase V8 and Paltrase MT 20 then further as "Pancrelipase", but no reference to the drug being marketed anywhere in the world.
- Palipase as Palipase, Palipase MT 16 and Palipase MT 20 then further as "Pancrelipase", but no reference to the drug being marketed anywhere in the world.

- Protilase as “Pancrelipase”, but no reference to the drug being marketed anywhere in the world.
  and
- Papase is listed as papain, which is marketed in Hong Kong.

Based on the lack of availability in the US market, we do not consider these names as potentially problematic. In reviewing the proprietary names available in the US market, we provide the following assessment.

1. Panokase contains lipase, protease and amylase indicated for enzyme replacement therapy in patients with deficient exocrine pancreatic secretions, such as in cystic fibrosis, chronic pancreatitis, postpancreatectomy, ductal obstructions caused by cancer of the pancreas or common bile duct, pancreatic insufficiency, and for steatorrhea of malabsorption syndrome and postgastrectomy or post-GI surgery. Panokase is available as “Panokase” and “Panokase 16”, with recommended dosing of one to four tablets with meals for cystic fibrosis and chronic pancreatitis patients and one to two tablets every 2 hours for pancreatectomy or obstruction of pancreatic ducts.

   The phonetic similarities stem from the shared three syllable count, leading “Pan”, and concluding “ase” sound. However, the central “tan” syllable of Patanase compared to the “ō” of Panokase should help to differentiate the two in speech. The orthographic similarities also stem from the shared leading letters “Pan” and concluding letters of “ase.” However, the central “tan” syllable of Patanase lengthens the name compared to the “o” of Panokase, which should help differentiate the two upon scripting.

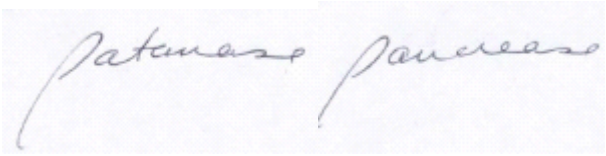


   Panokase is available in two strengths. The higher strength is indicated by the use of the modifier “16”. Thus for correct entry and order completion of this product, the modifier must be present or stated. Because this information will likely be included on a prescription, we do not consider Panokase 16 and Patanase problematic. However, Panokase and Patanase are single-strength products and an order for either would not need the strength to be written or stated for correct order completion. Despite this similarity, the products differ in route of administration (oral compared to intranasal), dosing frequency (with each meal/snack compared to twice daily), dosage form (tablets compared to nasal spray), order amount (usually multiple hundreds of tablets compared to #1/one bottle/30.5 grams) and indication of use (digestive enzyme replacement compared to symptoms associated with seasonal allergies and allergic rhinitis). Due to poor orthographic and phonetic similarities, in the presence of differing dosage forms, routes of administration, strengths (when present), and dispensing amounts, DMETS believes the possibility for confusion to be minimal.

2. Pancrease contains lipase, protease and amylase indicated for enzyme replacement therapy in patients with deficient exocrine pancreatic secretions, such as in cystic fibrosis, chronic pancreatitis, postpancreatectomy, ductal obstructions caused by cancer of the pancreas or common bile duct, pancreatic insufficiency, and for steatorrhea of malabsorption syndrome and postgastrectomy or post-GI surgery. Pancrease is available as “Pancrease”, “Pancrease MT 4”, “Pancrease MT 10”, Pancrease MT 16” and “Pancrease MT 20” with recommended dosing of 2,000 to 4,000 lipase units/120 mL of formula or breast milk for infants up to 12 months, 1000 lipase units/kg/meal to a maximum of 2,500 lipase units/kg/meal for children under 4 years of age and 400 lipase units/kg/meal up to a maximum of 2,500 lipase units/kg/meal for patients over 4 years of age.

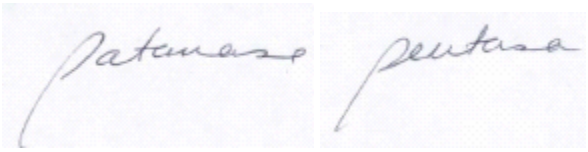
   The phonetic similarities stem from the shared three syllable count, leading “Pa” and concluding “ase” sound. However, the differences in the second syllable “crē” of Pancrease compared to

“tan” of Patanase differentiates the two names in speech. The orthographic similarities root in the shared leading letters “Pa” and concluding letters “ase.” However, the upstroke of the “t” in Patanase aids in name distinguishing upon scripting.



Pancrease is available in five strengths. Four of the strengths include the modifier of MT with a further numerical indicator (4, 10, 16, and 20). Thus for correct entry and order completion of these four products, the modifier must be present or stated. Because this information will likely be included on a prescription, we do not consider the Pancrease MT products and Patanase problematic. However, Pancrease and Patanase are single-strength products and an order for either would not need the strength to be written or stated for correct order completion. Despite this similarity, the products differ in multiple characteristics important for order completion such as route of administration (oral compared to intranasal), dosing frequency (with each meal/snack compared to twice daily), dosage form (capsules compared to nasal spray), order amount (usually multiple hundreds of capsules compared to #1/one bottle/30.5 grams), and indication of use (digestive enzyme replacement compared to symptoms associated with seasonal allergies and allergic rhinitis). Due to weak orthographic and phonetic similarities in the presence of differing dosage forms, routes of administration, strengths (when present), and dispensing amounts, DMETS believes the possibility for confusion to be minimal.

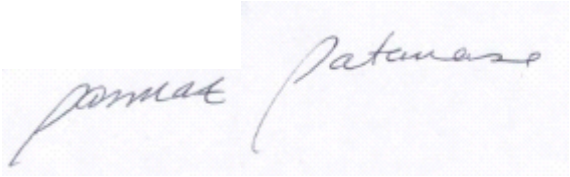
3. Pentasa contains mesalamine as a controlled-release capsule, which is indicated for the remission and treatment of mild to moderate active ulcerative colitis. The recommended dosing is one gram four times daily. Treatment duration was 8 weeks in clinical trials. The drug product is available as 250 mg and 500 mg capsules. The phonetic similarities stem from the shared three syllable count, leading “P” and central “t.” However, the concluding “əsə” of Pentasa is distinct in speech from the “anase” of Patanase. The orthographic similarities root in the similar leading “Pent” and “Pat” with the identical central “t” upstroke. However, the length of the concluding “asa” compared to “anase” should help differentiate upon scripting.



In addition, the drugs share no overlapping product characteristics as shown by the following: strength (250 mg and 500 mg compared to 665 mcg or no strength present on a prescription), route of administration (oral compared to intranasal), dosing frequency (four times daily compared to twice daily), dosage form (capsules compared to nasal spray), order amount (usually #240 or a number of capsules compared to #1/one bottle/30.5 grams), and indication of use (ulcerative colitis compared to symptoms associated with seasonal allergies and allergic rhinitis). Due to weak orthographic and phonetic similarities in the presence of many differing product characteristics, DMETS believes the possibility for confusion to be minimal.

4. Pannaz may look and sound similar to Patanase when scripted and spoken. Pannaz contains pseudoephedrine, carbinoxamine, and methscopolamine for the relief of symptoms associated with seasonal or perennial allergic rhinitis and vascular rhinitis, such as acute nasal and sinus congestion, sneezing, runny nose and postnasal drip and watery, itchy eyes. The recommended dose is one tablet twice daily for adults and ½ tablet every 12 hours for children ages 6 to 12. There is also a syrup available (Pannaz S), which should be dosed at one to two teapoonsful 4 times a day.

The phonetic similarities stem from the shared leading “P” and possible cognitive with “naz” and “nase.” However, the names differ in syllable count (two compared to three) and pivotal central phonemes (“n” compared to “t”). The orthographic similarities root in the shared leading “P.” The remainder of the names differ significantly with the double “nn” of Pannaz compared to the “tan” of Patanase and concluding “z” of Pannaz, which is distinct upon scripting compared to the “ase” of Patanase. In addition, Patanase is significantly longer due to the eight letter count compared to the six of Pannaz.



Pannaz is available in two dosage forms (tablets and syrup), with the proprietary name of the syrup including the modifier of “S.” Thus, for correct entry and order completion of Pannaz S, the modifier must be present or stated. . Because this information will likely be included on a prescription, we do not consider the Pannaz S and Patanase problematic. However, Pannaz and Patanase are single-strength products and an order for either drug product does not require the strength to be present for correct order completion. In addition, the drug products share the dosing frequency of twice daily. Despite this similarity, the products differ in multiple characteristics important for order completion such as route of administration (oral compared to intranasal), dosage form (tablets compared to nasal spray), and order amount (number of tablets compared to #1/one bottle/30.5 grams). Due to poor orthographic and phonetic similarities, in the presence of differing dosage forms, routes of administration, strengths (when present), and dispensing amounts, DMETS believes the possibility for confusion to be minimal.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Kimberly Culley-Pedersen
12/1/2005 12:03:25 PM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
12/1/2005 12:52:23 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
12/1/2005 01:30:53 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, DMETS Director, in her absence

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**ODS CONSULT #'s:**
February 27, 2003	July 18, 2003	03-0091, 03-0091-1
DOCUMENT DATE:	**PDUFA DATE:**	
February 17, 2003	October 7, 2005	

TO: Badrul Chowdhury, MD
Director, Division of Pulmonary and Allergy Drug Products
HFD-570

THROUGH: Anthony Zeccola
Project Manager, Division of Pulmonary and Allergy Drug Products
HFD-570

PRODUCT NAME:	**NDA SPONSOR:** Alcon Research
Patanase (Olopatadine Hydrochloride) Nasal Spray 665 mcg/spray **NDA#: 21-861**	

SAFETY EVALUATOR: Kimberly Culley, RPh

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Patanase. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

2. DMETS recommends implementation of the insert 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 proprietary name Patanase acceptable from a promotional perspective.

Denise Toyer, PharmD
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety

Carol Holquist, RPh
Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 5, 2005

NDA# 21-861

NAME OF DRUG: **Patanase** (Olopatadine Hydrochloride) Nasal Spray
665 mcg/spray

NDA HOLDER: **Alcon Research**

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

I. INTRODUCTION:

This consult was written in response to a request from the Division of Pulmonary and Allergy Drug Products (HFD-570) for an assessment of the proprietary name Patanase in regard to potential name confusion with other proprietary and/or established drug names. Container labels, carton and insert labeling were provided for review and comment. Additionally, the sponsor submitted a synopsis of a name validation study conducted by (b) (4) which is addressed by DMETS in Section II (E).

PRODUCT INFORMATION

Patanase (Olopatadine Hydrochloride) Nasal Spray is indicated for the (b) (4) treatment of the symptoms associated with seasonal (b) (4) allergic rhinitis in patients 12 years of age and older. Each metered spray delivers 665 micrograms of olopatadine, equivalent to 600 mcg of olopatadine base. Patanase will be supplied in a 30.5 gram metered-dose manual spray pump that contains 240 sprays. The recommended dose is two sprays in each nostril twice daily.

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] for existing drug names which sound-alike or look-alike to Patanase 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[4]. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS

[1] MICROMEDEX Integrated Index, 2004, 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, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.
[4] WWW location http://tess2.uspto.gov/bin/gate.exe?f=searchstr&state=m2pu5u.1.1

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 Patanase. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Error Prevention Staff with representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical skill, professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name Patanase acceptable from a promotional perspective.

2. Ten names were identified by the Expert Panel and independent review that were thought to have the potential for confusion with Patanase. These products with the available dosage forms and usual dosage are listed in table 1 (see page 4).

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel and Independent Review

Product Name	Established name, Dosage Form(s), Strength(s)	Usual adult dose*	Other**
Patanase	Olopatadine HCl Nasal Spray 665 mcg per spray	2 sprays in each nostril twice daily	
Beconase AQ®	Beclomethasone Dipropionate Monohydrate Nasal Spray, 42 mcg per spray	Adults: One to two sprays in each nostril twice daily. Children (6-12 years): One spray in each nostril twice daily; It is not recommended for children below 6 years of age. Maximum total daily dose: 2 sprays in each nostril twice daily (336 mcg/day).	SA
Betapace®	Sotalol Tablets, 80 mg, 120 mg, 160 mg, and 240 mg	Initial Dosing: Adults: 80 mg twice daily, up to 240 mg or 320 mg/day. Children: 30mg/m2 three times daily (max 60 mg/m2)	SA
Catarase	Chymortypsin Ophthalmic Solution, 150 units per vial and 300 units per vial	Discontinued from US, unable to locate dosing information	SA/LA
Patanol® Olopatadine Hydrochloride	Olopatadine Hydrochloride 0.1% Ophthalmic Solution, 5 mL 0.2%, 2.5 mL	One drop in affected eye two times daily. The interval between dosing should be six to eight hours. (0.2%) One drop in affected eye daily.	SA/LA
Retavase®	Reteplase Injection, 10.4 units per vial	Two ten unit bolus injections given over two minutes; the second injection is administered 30 minutes after the first injection.	LA
Vancenase® AQ DS Vancenase Pockethaler	Beclomethasone Dipropionate Monohydrate Nasal Spray, 84 mcg per spray Pockethaler, 42 mcg per spray	One to two sprays in each nostril daily	SA

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel and Independent Review			
Product Name	Established name, Dosage Form(s), Strength(s)	Usual adult dose*	Other**
Patanase	Olopatadine HCl Nasal Spray 665 mcg per spray	2 sprays in each nostril twice daily	
[redacted]			(b) (4)
Tolinase®	Tolazamide Tablets 100 mg, 250 mg and 500 mg	Initial dose: 100 mg-200 mg per day. Maintenance dose: 100 mg-1000 mg/day, average is 250 to 500 mg/day.	LA
Prohance®	Gadoteridol Injection 279.3 mg/mL Vials and Prefilled Syringes	0.1mmol/kg (0.2 mL/kg) as a rapid infusion or bolus	LA
[redacted]			(b) (4)
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike) *** **Name pending approval. Not FOI releasable.**			

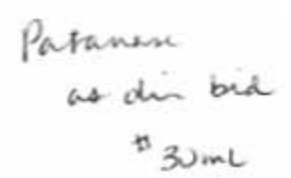
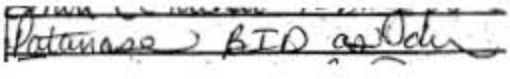
B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists that operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Patanase were captured by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Patanase with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 105 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 Patanase (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail and sent to a random sample of participating health professionals for their interpretation and review. After receiving either 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:	
	Patanase Twice daily as directed Thirty mls
Inpatient RX:	
	(*not verbatim, voice file unavailable)

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 for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Patanase, the primary concerns related to look-alike and sound-alike confusion with Beconase AQ, Vancenase AQ, Betapace, Patanol, Catarase, Retavase, (b) (4) Tolinase, Prohance, and (b) Catarase was discontinued from the U.S. market (formally removed July 1999 and May 2002) and does not appear to be available in a generic formulation. Thus, DMETS does not have concern with possible confusion. Upon further review of the names gathered from EPD and independent analysis, the names Prohance, Tolinase and Vancenase will not reviewed further because all Vancenase products appear to have been withdrawn from the U.S. market and Tolinase and Prohance differ in product strength, indication for use, frequency of administration, route of administration and dosage formulation.

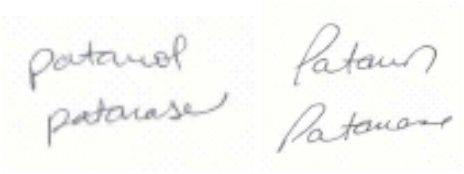
Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is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

1. Beconase AQ may sound similar to Patanase when spoken. Beconase AQ contains beclomethasone dipropionate, monohydrate for the relief of the symptoms associated with seasonal or perennial allergic, nonallergic (vasomotor) rhinitis and the prevention of recurrence of nasal polyps following surgical removal. The recommended dose for adults and children greater than twelve years of age is 1 or 2 nasal inhalations (42 to 84 mcg) in each nostril twice a day (total dose, 168 to 336 mcg/day). In children under 12 years of age, the dose is one nasal inhalation in each nostril twice daily, which may be increased to two inhalations in each nostril. Since Beconase AQ is the only currently marketed product in the “Beconase” line, the “AQ” does not need to be communicated for the patient to receive the correct medication. The auditory similarities stem from the shared ending

*** This is proprietary and confidential information that should not be released to the public.

"nase" and three syllable count. Verbally, the leading "Bec" and "Pat" should serve to distinguish the two names in speech. The verbal prescription studies conducted by DMETS found that all but one participant interpreted the leading syllable accurately. That one participant transposed the "t" and "p", therefore leading DMETS to interpret that the leading syllable should be distinguishable. The products share the overlapping characteristics of route of administration (nasal inhalation), dosage regimen (two nasal inhalations twice daily), and indication of use (relief of allergy symptoms). Although the products differ in strength (42 mcg per spray compared with 665 mcg per spray), strength may be omitted since each product will be available in one strength. Despite the many overlapping product characteristics, DMETS believes the chance of error to be minimal due to the lack of strong sound-alike similarity.

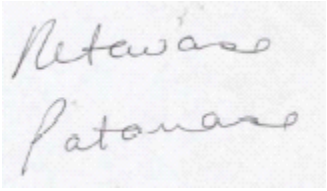
2. Betapace may sound similar to Patanase when spoken. Betapace contains sotalol for the treatment of arrhythmia and maintenance of normal sinus rhythm. The recommended dose is 80 mg twice daily, up to 240 mg or 320 mg. The verbal similarities result from the shared central syllable ("ta") and three syllable count, which is compounded by the similar concluding phonemes ('ace' and 'ase'). However, the different leading phonemes of "Be" compared with "Pa" and central "p" compared with "n" are distinct in speech, in Betapace and Patanase, respectively. In addition, they differ in most product characteristics including route of administration (oral compared with nasal), strength (80 mg, 120 mg, 160 mg and 240 mg compared with 665 mcg or 1 spray), dosage form (tablet compared with spray), dispensing amount (number of tablets compared with one bottle), and indication of use (arrhythmia compared with allergy symptoms). Although the products share frequency of dosing (twice daily), DMETS believes the possibility for name confusion to be minimal due to the numerous differing product characteristics.
3. Patanol may look and sound similar to Patanase when scripted and spoken. This new proposed drug product of Patanase contains the same active ingredient as in the currently marketed Patanol 0.1% and olapatadine 0.2% ophthalmic solutions. In addition, all three products are from the same sponsor, Alcon Research. Patanol contains olopatadine as a 0.1% ophthalmic solution for the treatment of allergic conjunctivitis. The recommended dose is one drop in each affected eye twice daily at an interval of 6 to 8 hours. In December 2004, olopatadine hydrochloride 0.2% solution (NDA 21-545) was approved for the ocular itching associated with allergic conjunctivitis and has been introduced into the marketplace. The recommended dose for olopatadine 0.2% is one drop in each affected eye once daily. Patanol 0.1% is available in a 5 mL bottle and the 0.2% olapatadine in a 2.5 mL bottle. The orthographic and auditory similarities stem from the shared leading "Patan" (see below). The concluding "ase" of Patanase should be distinguishable from "ol" of Patanol, especially in speech.



Due to the identical leading letters, the concern would be for practitioners to easily recognize the concluding letters upon scripting and in speech. Of note, practitioners have a verbal and orthographic association with "ase" due to the currently marketed nasal sprays, such as Beconase, Flonase, Nasonex, Nasarel and Nasacort. The DMETS verbal study helps to confirm that the phoneme of "nāz" is identifiable, since all the participants identified the concluding "ase" correctly. In addition, all of the inpatient participants and the majority of the outpatient participants identified the concluding "ase" correctly. There were six participants from the outpatient study that interpreted "ese." The products share frequency of dosing/dosing directions (twice daily/use as directed) and dispensing amount

(one bottle). In addition, physicians may indicate “use as directed or UD” for both the eye and nasal formulation of olopatadine. However, since ocular olopatadine exists in two strengths, the provider will likely indicate strength on the prescription, which should provide a differentiating characteristic. There is also the likelihood that practitioners will indicate ocular use or note which eye to instill the solution, which may serve as an additional method to differentiate. Furthermore, the products differ in route of administration (ocular compared with nasal), indication (signs and symptoms of allergic conjunctivitis, ocular itching associated with allergic conjunctivitis and management and treatment of the symptoms of season and perennial allergic rhinitis), dosing amount (one drop compared to two sprays), and drug presentation (solution in a dropper compared with closed container spray). DMETS acknowledges that the sponsor is requesting a dual tradename. However, after consulting with the medical officer, systemic absorption of both drug products would not result in patient harm as oral studies revealed only minor side effects with approximately seventeen times the recommended nasal dose. Thus, there appears to be little safety concern when the two products are used concomitantly. Additionally, Patanase follows the traditional naming convention that other products use to differentiate their nasal preparations from their orally inhaled formulations (i.e. Beclovent/Beconase and Vanceril/Vancenase). Due to the differing route of administrations, orthographic and verbal differences, DMETS believes the possibility for confusion to be minimal.

4. Retavase may look and sound like Patanase when scripted or spoken. Retavase contains reteplase as an injection for the management of acute myocardial infarction by improving ventricular function following myocardial infarction, reducing the incidence of congestive heart failure and reducing mortality. The recommended dose is a double-bolus 10 unit injection. The orthographic similarities result from the shared central “t”, concluding “ase”, and the likeness of “v” compared to “n” and the leading “R” compared to “P” when scripted (see below).



The auditory similarities stem from the shared central “tă” sound and concluding “ase.” However, the leading “R” compared to “P” should create a distinct characteristic in speech, in addition to the central “v” of Retavase. Although the products share single strength status (10.4 units compared with 664 mcg/1 spray), they differ in the remaining characteristics as seen by the following: route of administration (intravenous compared with nasal inhalation), dose (two, ten bolus units compared with one to two sprays), dosing frequency (single administration compared with twice daily), duration of therapy (one time use compared with maintenance therapy), and indication (myocardial infarction compared with allergy control). Although the product names share a significant resemblance on scripting, the context of use and differing characteristics should help to diminish name confusion.

5. (b) (4)

*** This is proprietary and confidential information that should not be released to the public.

(b) (4)

6. (b) (4)

(b) (4)

E. INDEPENDENT NAME ANALYSIS (b) (4)

The sponsor submitted a letter providing information on a name validation study conducted by (b) (4) The study involved ten proposed trademarks, including Patanase. (b) (4) found that the name, Patanase, was acceptable as a trademark for the nasal formulation of olopatadine HCl. (b) (4) provided the following four data points to support this conclusion (see below). DMETS will respond only to datapoints where specifics or background information were provided, not just conclusions.

- Not one of the 74 healthcare professionals who participated in the unaided simulated verbal order evaluation misinterpreted Patanase for an existing product name.

- 61 of the 63 healthcare professionals who participated in an unaided simulated written order evaluation did not misinterpret Patanase for an existing product name. While one physician and one pharmacist misinterpreted the name as Patanol, the name was correctly interpreted by 68% of the respondents and there were no additional misinterpretations for any other existing product names in the evaluation.

DMETS response: (b) (4) This new step in oral and written prescriptions will serve as a differentiating characteristic.

- 75% of the 212 healthcare professional samples assess Pantanase as ‘Suitable’ to represent the new nasal formulation of olopatadine HCl, the highest percentage of the ten names tested.

- Only 7% of the professionals sampled said that Patanase was ‘Unsuitable’, the lowest percentage of the ten names tested. Of these respondents, no one cited “potential for

misprescription with an existing/specific product name' beyond general perceptual similarity to the ophthalmic formulation of Patanol.

DMETS response: DMETS acknowledges and concurs with the results of the name validation study that Patanase is a suitable name for this product.

III. LABELING AND SAFETY RELATED ISSUES:

In the review of the insert labeling of Patanase, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement that may minimize potential user error.

A. CARTON LABELS AND CONTAINER LABELING

1. Please revise the established name to read as follows (i.e. to include chemical name and dosage form):

   Olopatadine Hydrochloride Nasal Spray

2. Increase the prominence of the "FOR NASAL USE ONLY" warning, by changing the color and/or increasing the font size. This will help to alleviate confusion with the ophthalmic formulation of olopatadine (Patanol).

3. Decrease or remove the graphic art (e.g. the red inhaler image) as this is distracting from the proprietary and established name.

4. Revise the font color to black for the information on the carton and container labels. As currently presented, the blue font does not contrast enough on the fading blue background, thus making the verbiage difficult to read.

5. Due to the co-existence of this nasal product with the ocular product in the marketplace consider the addition of a visual cue to the route of administration. This could be a direct or background image (e.g. watermark look) of a nose.

B. CONTAINER LABELS

1. Please add "Only" to the "For Nasal Use" as seen on the Carton Labeling.

C. PACKAGE INSERT

1. Dosage and Administration Section

   Please add this paragraph "After initial priming (5 sprays)……provides 240 sprays after priming." from the Description Section to the Dosage and Administration per 21 CFR 201.57(j).

C. Patient's Instructions for Use

(b) (4)

IV. RECOMMENDATIONS:

A. DMETS has no objections to the use of the proprietary name, Patanase. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

B. 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.

C. DDMAC finds the proprietary name Patanase 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 Sammie Beam, project manager, at 301-827-2102.

_____

Kim Culley, RPh
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

_____

Alina Mahmud, RPh, MS
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A: DMETS Prescription Study Results (Patanase)

Inpatient	**Outpatient**	**Voice**
Patanase	Patanase	Patinase
Patanase	Patanase	Patinase
Patanase	Patanase	Patinase
Patanase	Patanase	Patanase
Patanase	Patanase	Patanase
Patanase	Patanase	Patenase
Patanase	Paranese	Patonase
Patanase	Patanase	Pantanase
Patanase	Patarese	Patinase
Patanase	Patanase	Patanase
Patanase	Patanase	Patinase
Patanase	Potanese	Patenase
Patanase	Patanase	Tepanase
Patanase	Patanase	Patanase
Patanase	Patanase	Patanase
Patanase	Patanese	
Patanase	Patanase	
Patanase	Patanese	
Patanase	Patanese	
Datanase		
Patanase		
Patanase		
Patanase		

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Kimberly Culley
8/12/05 08:37:03 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
8/12/05 09:23:36 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
8/12/05 12:43:26 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
8/12/05 01:18:06 PM
DRUG SAFETY OFFICE REVIEWER