

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number 21-231**

**ADMINISTRATIVE DOCUMENTS**  
**CORRESPONDENCE**

**APPROVAL PACKAGE**  
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**Zomig -ZMT**  
**(Zolmitriptan Orally Disintegrating Tablets)**  
**NDA 21-231**

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**Outside of Approval Package**

Approval Letter/Labeling

**Inside of Approval Package (1 volume)**

**General Information:**

- A. Action Package Checklist
- B. Action Letter (copy)
- C. Labeling
  - OPDRA Proprietary Name Review
  - Draft Insert - Division
  - Draft Insert - Sponsor
  - Carton and Container Labeling (draft)
- D. Correspondence, Telecon Memos
- E. Post-Marketing Commitments
- F. Patent Information
- G. Exclusivity Checklist
- H. Debarment Certification
- I. Financial Disclosure
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- L. Minutes of Meetings

**Clinical Information:**

- M. Summary Memoranda
- N. Clinical Review
- O. Pediatric Information
- P. Statistical Review
- Q. Biopharmaceutics / Clinical Pharmacology Review
- R. DSI Audits

**APPROVAL PACKAGE  
Table of Contents**

**Zomig -ZMT  
(Zolmitriptan Orally Disintegrating Tablets)  
NDA 21-231**

**CMC Information:**

- S. CMC Reviews and Memoranda
- T. Statistics reviews and memoranda (regarding dissolution and/or stability)
- U. DMF review
- V. EA review/FONSI/Categorical exemption
- W. Facilities Inspection

**Preclinical Pharm/Tox Information:**

- X. Pharmacology / Toxicology Review and Memoranda

**APPEARS THIS WAY  
ON ORIGINAL**

**NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST**

NDA <u>21-231</u> / SE _____ - _____	
Drug <u>Zomig-ZMT (zolmitriptan)</u>	Applicant: <u>Zeneca</u>
RPM <u>Lana Chen, R.Ph.</u>	Phone <u>301-594-5529</u>
<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Reference listed drug _____	
<input type="checkbox"/> Fast Track	<input type="checkbox"/> Rolling Review
Review priority: <input checked="" type="checkbox"/> S <input type="checkbox"/> P	
Pivotal IND(s) <u>IND 45,147, NDA 20-768</u>	
Application classifications:	PDUFA Goal Dates:
Chem Class <u>3S</u>	Primary <u>2/14/01</u>
Other (e.g., orphan, OTC) _____	Secondary <u>4/14/01</u>

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

**GENERAL INFORMATION:**

- ◆ User Fee Information:  User Fee Paid  
 User Fee Waiver (attach waiver notification letter)  
 User Fee Exemption
  
- ◆ Action Letter.....  AP  AE  NA
  
- ◆ Labeling & Labels
 

FDA revised labeling and reviews.....	X
Original proposed labeling (package insert, patient package insert) .....	X
Other labeling in class (most recent 3) or class labeling.....	X
Has DDMAC reviewed the labeling? .....	<input type="checkbox"/> Yes (include review) <input checked="" type="checkbox"/> No
Immediate container and carton labels .....	X
Nomenclature review .....	X
  
- ◆ Application Integrity Policy (AIP)  Applicant is on the AIP. This application  is  is not on the AIP.
 

Exception for review (Center Director's memo).....	
OC Clearance for approval.....	

- ◆ Status of advertising (if AP action)  Reviewed (for Subpart H – attach review) ■ Materials requested in AP letter
  
- ◆ Post-marketing Commitments
  - Agency request for Phase 4 Commitments.....
  - Copy of Applicant’s commitments .....
  
- ◆ Was Press Office notified of action (for approval action only)?.....  Yes  No
  - Copy of Press Release or Talk Paper.....
  
- ◆ Patent
  - Information [505(b)(1)] ..... X
  - Patent Certification [505(b)(2)].....
  - Copy of notification to patent holder [21 CFR 314.50 (i)(4)].....
  
- ◆ Exclusivity Summary ..... X
  
- ◆ Debarment Statement ..... X
  
- ◆ Financial Disclosure
  - No disclosable information ..... X
  - Disclosable information – indicate where review is located .....
  
- ◆ Correspondence/Memoranda/Faxes ..... X
  
- ◆ Minutes of Meetings .....
  - Date of EOP2 Meeting \_\_\_\_\_
  - Date of pre NDA Meeting \_\_\_\_\_
  - Date of pre-AP Safety Conference \_\_\_\_\_
  
- ◆ Advisory Committee Meeting ..... N/A
  - Date of Meeting .....
  - Questions considered by the committee .....
  - Minutes or 48-hour alert or pertinent section of transcript .....
  
- ◆ Federal Register Notices, DESI documents ..... N/A

**CLINICAL INFORMATION:**

**Indicate N/A (not applicable), X (completed), or add a comment.**

- ◆ Summary memoranda (e.g., Office Director’s memo, Division Director’s memo, Group Leader’s memo) ..... X
  
- ◆ Clinical review(s) and memoranda ..... X

- ◆ Safety Update review(s) ..... X \_\_\_\_\_
- ◆ Pediatric Information
  - Waiver/partial waiver (Indicate location of rationale for waiver)  Deferred Pediatric Page..... X \_\_\_\_\_
  - Pediatric Exclusivity requested?  Denied  Granted  Not Applicable
- ◆ Statistical review(s) and memoranda ..... X \_\_\_\_\_
- ◆ Biopharmaceutical review(s) and memoranda..... X \_\_\_\_\_
- ◆ Abuse Liability review(s) ..... N/A \_\_\_\_\_  
 Recommendation for scheduling .....
- ◆ Microbiology (efficacy) review(s) and memoranda ..... N/A \_\_\_\_\_
- ◆ DSI Audits ..... X \_\_\_\_\_
  - Clinical studies  bioequivalence studies .....

**CMC INFORMATION:**

Indicate N/A (not applicable), X (completed), or add a comment.

- ◆ CMC review(s) and memoranda ..... X \_\_\_\_\_
- ◆ Statistics review(s) and memoranda regarding dissolution and/or stability .....
- ◆ DMF review(s) .....
- ◆ Environmental Assessment review/FONSI/Categorical exemption .....
- ◆ Micro (validation of sterilization) review(s) and memoranda .....
- ◆ Facilities Inspection (include EES report)
  - Date completed \_\_\_\_\_  Acceptable  Not Acceptable
- ◆ Methods Validation .....  Completed  Not Completed

**PRECLINICAL PHARM/TOX INFORMATION:**

Indicate N/A (not applicable), X (completed), or add a comment.

- ◆ Pharm/Tox review(s) and memoranda ..... X \_\_\_\_\_
- ◆ Memo from DSI regarding GLP inspection (if any) ..... X \_\_\_\_\_

- ◆ Statistical review(s) of carcinogenicity studies ..... X \_\_\_\_\_
- ◆ CAC/ECAC report ..... X \_\_\_\_\_

**APPEARS THIS WAY  
ON ORIGINAL**

**FOOD AND DRUG ADMINISTRATION  
DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS  
(HFD-120)  
5600 FISHERS LANE  
ROCKVILLE, MARYLAND 20857  
FAX (301) 594-2859**

**Telecopier Cover Sheet**

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**DATE:** February 13, 2001

**TIME:**

**DELIVER TO:** Ms. Patricia DeFeo

**Fax Number:** (302) 886-2822

**FROM:** Lana Chen, R. Ph.  
Regulatory Management Officer  
Ph 301-594-5529

**Total number of pages, including cover page: 32**

If you do not receive all pages or have any problems with receiving, call (301) 594-2850.

**MESSAGE:**

**Pat,**

**RE: NDA 21-231 ——— (Zolmitriptan) Orally Disintegrating Tabs**

**Please see attached Approval Letter and Labeling.**

**Thanks,  
Lana**

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

**DATE RECEIVED:** January 8, 2001

**DUE DATE:** February 14, 2001

**OPDRA CONSULT #:** 01-0004

**TO:** Russell G. Katz, M.D.  
Director, Division of Neuropharmacological Drug Products  
HFD-120

**THROUGH:** Lana Chen, Project Manager  
HFD-120

**PRODUCT NAME:** Zomig ZMT,  
\_\_\_\_\_ (zolmitriptan orally  
disintegrating tablets; 2.5mg)

**NDA #:** 21-231

**MANUFACTURER:** Zeneca Pharmaceuticals  
1800 Concord Pike  
P.O. Box 15437  
Wilmington, DE 19850-5437

**SAFETY EVALUATOR:** Carol Pamer, R.Ph.

**SUMMARY:** In response to a consult request from the Division of Neuropharmacological Drug Products (HFD-120), OPDRA conducted a final review of the proposed proprietary names "Zomig ZMT" and \_\_\_\_\_ to determine the potential for confusion with approved proprietary and generic names as well as pending names.

**OPDRA RECOMMENDATION:** From a safety perspective, OPDRA does not object to the use of the name \_\_\_\_\_. We do not recommend use of the name "Zomig ZMT". See the checked box below.

**FOR NDA/ANDA WITH ACTION DATE BEYOND 90 DAYS OF THIS REVIEW**

This name 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 names/NDAs from the signature date of this document. A re-review request of the name should be submitted via e-mail to "OPDRAREQUEST" with the NDA number, the proprietary name, and the goal date. OPDRA will respond back via e-mail with the final recommendation.

**FOR NDA/ANDA WITH ACTION DATE WITHIN 90 DAYS OF THIS REVIEW**

OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDAs from this date forward.

**FOR PRIORITY 6 MONTH REVIEWS**

OPDRA will monitor this name until approximately 30 days before the approval of the NDA. The reviewing division need not submit a second consult for name review. OPDRA will notify the reviewing division of any changes in our recommendation of the name based upon the approvals of other proprietary names/NDAs from this date forward.

\_\_\_\_\_  
Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment  
Phone: (301) 827-3246  
Fax: (301) 480-8173

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

**Office of Postmarketing Drug Risk Assessment (OPDRA)**

**HFD-400; Parklawn Building Room 15B-03**

**FDA Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** January 18, 2001

**NDA NUMBER:** 21-231

**NAME OF DRUG:** Zomig ZMT and \_\_\_\_\_  
(zolmitriptan orally disintegrating tablets, 2.5mg)

**NDA HOLDER:** Zeneca Pharmaceuticals  
1800 Concord Pike  
P.O. Box 15437  
Wilmington, DE 19850-5437

**I. INTRODUCTION**

This consult was written in response to a request from the Division of Neuropharmacological Drug Products (HFD-120) for final assessment of the tradenames Zomig ZMT and \_\_\_\_\_. The sponsor has submitted no additional data supporting the use of either trade name at this time. Draft packaging and labeling (e.g., carton and blister labels) have been included with Revision date of March 16, 2000.

A previous review of the tradenames names "Zomig ZMT" and \_\_\_\_\_ was completed on February 23, 2000 by OPDRA (see OPDRA consult 99-109). The primary concerns raised were related to the name "Zomig ZMT". These concerns were specifically the use of a suffix which has no discernible meaning and the potential for the "Z" to be mistaken for a "2". These concerns were supported by prescription analysis studies we conducted; 7 of 19 respondents interpreted the "Z" as a "2". *For these reasons, we objected to the use of the name Zomig ZMT for this product.*

\_\_\_\_\_ was evaluated as an alternative to "Zomig ZMT". In the prescription studies, there were some misinterpretations of this name with Soma and Zomax (no longer marketed in the U.S.). However, confusion of Soma with \_\_\_\_\_ seems unlikely since there are no overlapping strengths with Soma (carisoprodol 350mg). Some prescription study participants interpreted the handwritten suffix \_\_\_\_\_ as "Pedi" or "Pediatric". *From a safety perspective, we did not object to the use of the proprietary name \_\_\_\_\_.* Note also that one product with a similar modifier name for a like dosage form is already marketed in the U.S.: Claritin Reditabs™. This product, approved on December 23, 1996, is a tablet dosage form described as an "orally disintegrating tablet" as is the subject drug of NDA 21-231,

Zomig ZMT/ \_\_\_\_\_ is an orally disintegrating tablet containing 2.5mg zolmitriptan. Zolmitriptan is a selective 5-hydroxytryptamine receptor agonist which is indicated for the acute treatment of migraine with or without aura in adults. On November 25, 1997, the Division of Neuropharmacological Drug

Products approved Zomig™, zolmitriptan 2.5 and 5-mg standard tablets, for treatment of acute migraine. In clinical trials, the usual effective adult dose of the standard tablet dosage form of Zomig was a single dose ranging from 1 to 5 mg. The FDA-approved labeling for Zomig recommends a starting dose of 2.5 mg or lower. The dose may be repeated after 2 hours if headache returns, not to exceed 10 mg per 24 hour-period.

## II. RISK ASSESSMENT

The medication errors staff of OPDRA conducted a search of several standard published drug product reference texts<sup>1,2,3</sup> as well as several FDA databases<sup>4</sup> for existing drug names which sound alike or look alike to Zomig ZMT and \_\_\_\_\_ to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>5</sup>. An Expert Panel discussion was conducted to review all findings from the searches. The primary emphasis of the searches was on sound-alike, look-alike proprietary names that may have been approved since the initial OPDRA review of these two product names in February of 2000.

### A. EXPERT PANEL DISCUSSION

A group discussion was held by OPDRA to gather professional opinions on the safety of a proprietary name. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of FDA health professionals (pharmacists) from OPDRA and the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

No additional sound-alike, look alike proprietary names were identified by the Expert Panel. Again, the primary concerns with the two proposed proprietary names related to the name "Zomig ZMT". The use of suffixes that do not have some discernible meaning is generally discouraged. Also, "Z" is often mistaken for a 2 in the usual prescription ordering process, which may be mistaken for "2 mg" or "2" tablets. For these reasons and in the absence of other data submitted by the sponsor in support of either name, a consensus was formed that there are safety concerns with the use of the name "Zomig ZMT". There were no significant objections based on safety concerns related to the use of the name \_\_\_\_\_.

In addition, DDMAC did not object to the name \_\_\_\_\_, based on promotional concerns.

### B. SAFETY EVALUATOR RISK ASSESSMENT

As in our previous review of the proprietary names "Zomig ZMT" and \_\_\_\_\_, the primary concerns raised were related to the name "Zomig ZMT". These concerns were specifically the use of a suffix that has no discernible meaning. The potential also was thought to exist for the "Z" to be mistaken

<sup>1</sup> MICROMEDEX Healthcare Intranet Series, 2001, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Emergindex, Reprodisk, index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc).

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

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

<sup>4</sup> COMIS. New Drug Approvals 99-01, and the electronic online version of the FDA Orange Book.

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

for a "2", leading to administration of 2-Zomig tablets or possibly "ZMT" being interpreted as "2 MG" (see following illustration).

Handwritten text "Zomig Zmt" in cursive script.

Handwritten text "Zomig Zmo" in cursive script.

We conducted prescription studies in our previous review in an attempt to simulate the prescription ordering process. In this case, there was some confirmation that the handwritten "Z" would be mistaken for a "2". For these reasons, we object to the use of the name Zomig ZMT for this product.

\_\_\_\_\_ was evaluated as an alternative to Zomig ZMT and was not believed to present a significant safety concern. Therefore, we do not object to the use of the proprietary name " \_\_\_\_\_

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

In the review of the carton labeling and container labels (blister packs) for Zomig ZMT/ \_\_\_\_\_ JDPRA has maintained a focus on safety issues related to possible medication errors. *There were no significant safety concerns noted in the materials provided*, which included carton labels for 6-tablet blister packs and the container labels for the same packaging configuration.

### IV. RECOMMENDATIONS

From a safety perspective, OPDRA has no objections to the use of the proprietary name \_\_\_\_\_ We do not recommend use of the name "Zomig ZMT".

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Carol Pamer, R.Ph. at 301-827-3242.

---

Carol Pamer, R.Ph.  
Safety Evaluator  
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

---

Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Postmarketing Drug Risk Assessment (OPDRA)

L:\OPDRA01\PAMER\FINAL CONSULTS\010004ZOMIGZMT.FIN.DOC

/s/

-----  
Carol Pamer  
1/25/01 04:27:55 PM  
PHARMACIST

Jerry Phillips  
1/26/01 08:15:13 AM  
DIRECTOR

Martin Himmel  
1/29/01 12:58:56 PM  
MEDICAL OFFICER

**APPEARS THIS WAY  
ON ORIGINAL**

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

**DATE RECEIVED:** December 10, 1999

**DUE DATE:** Not specified

**OPDRA CONSULT #:** 99-109

**TO:** Russell G. Katz, M.D.  
Director, Division of Neuropharmacological Drug Products (HFD-120)  
HFD-120

RECEIVED FEB 28 2000  
FEB 28 2000

**THROUGH:** Lana Chen, Project Manager  
HFD-120

**PRODUCT NAME:** Zomig ZMT, \_\_\_\_\_  
\_\_\_\_\_ (zolmitriptan orally disintegrating tablets;  
2.5mg)

**MANUFACTURER:** Zeneca Pharmaceuticals  
1800 Concord Pike  
P.O. Box 15437  
Wilmington, DE 19850-5437

**SAFETY EVALUATOR:** Carol Pamer, R.Ph.

**SUMMARY:** In response to a consult from the Division of Neuropharmacological Drug Products (HFD-120), OPDRA conducted a review of the proposed proprietary names "Zomig ZMT" and \_\_\_\_\_ to determine the potential for confusion with approved proprietary and generic names as well as pending names.

**OPDRA RECOMMENDATION:** From a safety perspective, OPDRA has no objections to the use of the name \_\_\_\_\_". We do not recommend use of the name "Zomig ZMT".

This is considered a tentative decision and the firm should be notified that this name must be re-evaluated 90 days prior to the expected approval of the NDA. A re-review of the name prior to the NDA approval will rule out any objections based upon approvals of other proprietary names/NDAs from this date forward. An outline of how the firm intends to \_\_\_\_\_ could also be suggested.

JS 2/23/2000  
Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Post-Marketing Drug Risk Assessment  
Phone: (301) 827-3246  
Fax: (301) 480-8173

JS 2/23/00  
Peter Honig, M.D.  
Deputy Director  
Office of Post-Marketing Drug Risk Assessment  
Center for Drug Evaluation and Research  
Food and Drug Administration

**Office of Postmarketing Drug Risk Assessment (OPDRA)**

**HFD-400; Parklawn Building Room 15B-03**

**FDA Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** February 18, 2000

**IND NUMBER:** \_\_\_\_\_

**NAME OF DRUG:** Zomig ZMT and \_\_\_\_\_  
(zolmitriptan orally disintegrating tablets, 2.5mg)

**IND HOLDER:** Zeneca Pharmaceuticals  
1800 Concord Pike  
P.O. Box 15437  
Wilmington, DE 19850-5437

**I. EXECUTIVE SUMMARY**

In reviewing the proprietary names "Zomig ZMT" and \_\_\_\_\_, the primary concerns raised were related to the name "Zomig ZMT". These concerns were specifically the use of a suffix which has no discernible meaning and the potential for the "Z" to be mistaken for a "2". These concerns were supported by prescription analysis studies we conducted. For these reasons, we object to the use of the name Zomig ZMT for this product.

\_\_\_\_\_ was evaluated as an alternative to "Zomig ZMT". In the prescription studies, there were some misinterpretations of this name with Soma and Zomax (no longer marketed in the U.S.). However, confusion of Soma with \_\_\_\_\_/ZMT seems unlikely since there are no overlapping strengths with Soma (carisoprodol 350mg). Some prescription study participants interpreted the handwritten suffix '\_\_\_\_\_' as "Pedi" or "Pediatric". Education of health professionals prior to distribution of this new "Zomig"-line product will be important to avoid medication errors. From a safety perspective, we do not object to the use of the proprietary name '\_\_\_\_\_'

**II. INTRODUCTION**

This consult was written in response to a request from the Division of Neuropharmacological Drug Products (HFD-120) for assessment of the tradenames Zomig ZMT and \_\_\_\_\_

Zomig ZMT/ \_\_\_\_\_ is an orally disintegrating tablet containing 2.5mg zolmitriptan. Zolmitriptan is a selective 5-hydroxytryptamine receptor agonist which is indicated for the acute treatment of migraine with or without aura in adults. Draft product labeling was not available for Zomig \_\_\_\_\_/Zomig ZMT (zolmitriptan orally disintegrating tablets) at the time of this review.

On November 25, 1997, the Division of Neuropharmacological Drug Products approved Zomig™, zolmitriptan 2.5 and 5-mg tablets, for treatment of acute migraine. In clinical trials, the usual effective adult dose of the standard tablet dosage form of Zomig was a single dose ranging from 1 to 5 mg. The FDA-approved labeling for Zomig recommends a starting dose of 2.5 mg or lower. The dose may be repeated after 2 hours if headache returns, not to exceed 10 mg per 24 hour-period.

### III. RISK ASSESSMENT

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts<sup>iii,iii</sup> as well as several FDA databases<sup>iv</sup> for existing drug names which sound alike or look alike to Zomig ZMT and \_\_\_\_\_ to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>v</sup>. An Expert Panel discussion was conducted to review all findings from the searches. In addition, OPDRA conducted 4 prescription analysis studies, to simulate the prescription ordering process.

#### A. EXPERT PANEL DISCUSSION

A group discussion was held by OPDRA to gather professional opinions on the safety of a proprietary name. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of FDA health professionals (pharmacists) from OPDRA and the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

Because Zomig tablets are already marketed in the U.S., the focus of the discussion related to the two suffixes proposed by the manufacturer. The primary concerns with the two proposed proprietary names were associated with the name "Zomig ZMT". The use of suffixes that do not have some discernible meaning is generally discouraged. Also, "Z" is often mistaken for a 2 in the usual prescription ordering process, which may be mistaken for "2 mg" or "2" tablets. For these reasons, a consensus was formed that there are safety concerns with the use of the name "Zomig ZMT". There were no significant objections based on safety concerns related to the use of the name " \_\_\_\_\_".

Because \_\_\_\_\_ Zomig ZMT is a new dosage form being added to a product line with the same root name (e.g., Zomig), the sponsor should provide sufficient education prior to availability of this product to familiarize health care practitioners with this new product, as confusion may

<sup>i</sup> MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Emergindex, Reprodisk, index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 1999).

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

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

<sup>iv</sup> Drug Product Reference File [DPR], the Established Evaluation System [EES], the AMF Decision Support System [DSS], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-99, and the electronic online version of the FDA Orange Book.

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

occur between the existing product and a new product. Previous and more recent experience with medication errors have demonstrated that a lack of familiarity with a product added to an existing product line such as this can result in confusion when a prescription for the new product is received and possibly dispensed.

## B. STUDY CONDUCTED BY OPDRA

### 1. Methodology

A study was conducted within FDA employing a total of 93 health care professionals (nurses, pharmacists, physicians) to determine the degree of confusion of Zomig ZMT and Zomig Redi with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. This exercise was conducted in an attempt to simulate the prescription ordering process. An OPDRA staff member wrote outpatient prescriptions, each consisting of a combination of marketed and unapproved drug products and prescriptions for Zomig ZMT and \_\_\_\_\_ (see below). These written prescriptions were optically scanned and one prescription was delivered via email to each study participant. In addition, one OPDRA staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via email.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTIONS
Outpatient: _____, 1 p.o. p.r.n., #10	Outpatient: _____, take one tablet orally as needed, dispense 10
Outpatient: Zomig ZMT, i p.o. p.r.n., #10	Outpatient: Zomig ZMT, take one tablet orally as needed, dispense 10

### 2. Results

Results of this exercise are summarized below:

Study	No. of participants	# of responses (%)	"Zomig ZMT" or _____ response	Other response
Written: Zomig ZMT	23	19 (83%)	1 (5%)	18 (95%)
_____	24	18 (75%)	1 (5%)	17 (95%)
Verbal: Zomig ZMT	23	13 (57%)	6 (46%)	7 (54%)
_____	23	17 (74%)	0 (0%)	17 (100%)
Total	93	67 (72%)	8 (12%)	59 (88%)

#### a. \_\_\_\_\_

Among participants in the written prescription study, the majority of the respondents (95%) provided misspelled variations of the drug name; only one study participant interpreted the name as "\_\_\_\_\_\_\_\_\_\_". Interestingly, 3 respondents interpreted the name as a pediatric Zomig formulation, "Zomig Pedi" (n=2) and "Zomig Pediatric" (n=1).

Among verbal prescription study participants, none of the study participants interpreted the name correctly. Most of the name interpretations were phonetic variations of \_\_\_\_\_, with one response of "Zomig Ready". However, two respondents interpreted the name as "Soma Ready" and "Zomax".

b. Zomig ZMT

Among participants in the written prescription study, the majority of the respondents (95%) provided misspelled variations of the drug name; only one study participant interpreted the name as "Zomig ZMT". *Seven of nineteen respondents (37%) interpreted the suffix "ZMT" as "2 MT" or "2 mt". Two of 19 respondents (10%) interpreted the name as "Zomig" without the suffix, the existing U.S. product.*

Among verbal prescription study participants, a larger number interpreted the name correctly (6 of 13, 46%). Most of the incorrect name interpretations were phonetic variations of "Zomig ZMT". *Two of 13 respondents (15%) interpreted the name as "Zomig" without the suffix, the existing U.S. product.*

**C. SAFETY EVALUATOR RISK ASSESSMENT**

In reviewing the proprietary names "Zomig ZMT" and "          ", the primary concerns raised were related to the name "Zomig ZMT". These concerns were specifically the use of a suffix which has no discernible meaning and the potential for the "Z" to be mistaken for a "2". With either product name, a mechanism should be in place prior to distribution to inform health professionals of a new product with the root name "Zomig" so that confusion between the existing "Zomig" product does not occur. We conducted prescription studies in an attempt to simulate the prescription ordering process. In this case, there was some confirmation that the handwritten "Z" would be mistaken for a "2" and that the new product would be confused with the familiar product, Zomig. For these reasons, we object to the use of the name Zomig ZMT for this product.

           was evaluated as an alternative to Zomig ZMT. In the prescription studies, there were some misinterpretations of this name with Soma and Zomax (no longer marketed in the U.S.). However, confusion of Soma with            ZMT seems unlikely since there are no overlapping strengths with Soma (carisoprodol 350mg). A search of the FDA AERS database for all cases of medication errors with zolmitriptan was conducted; there were no cases where Zomig standard tablets have been confused with Soma.

An interesting finding was that some prescription study participants interpreted the handwritten suffix "          " as "Pedi" or "Pediatric". Again, education of health professionals prior to distribution of this new "Zomig"-line product will be important to avoid medication errors. From a safety perspective, we do not object to the use of the proprietary name           

APPEARS THIS WAY  
ON ORIGINAL

#### IV. RECOMMENDATIONS

From a safety perspective, OPDRA has no objections to the use of the proprietary name —  
— We do not recommend use of the name "Zomig ZMT".

This is considered a tentative decision and the firm should be notified that this name must be re-evaluated 90 days prior to the expected approval of the NDA. A re-review of the name prior to the NDA approval will rule out any objections based upon approvals of other proprietary names/NDAs from this date forward. An outline of how the firm intends to inform health professionals of a new "Zomig"-line product could also be suggested.

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Carol Pamer, R.Ph. at 301-827-3245.

*1st*  
\_\_\_\_\_  
Carol Pamer, R.Ph.  
Safety Evaluator  
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

*1st* *2/23/2000*  
\_\_\_\_\_  
Jerry Phillips, R.Ph.  
Associate Director for Medication Error Prevention  
Office of Postmarketing Drug Risk Assessment (OPDRA)

## MEMORANDUM

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

## CLINICAL INSPECTION SUMMARY

DATE: January 12, 2001

TO: Lana Chen, R. Ph., Regulatory Project Manager  
Armando Oliva, M.D., Clinical Reviewer  
Division of Neuropharmacological Drug Products, HFD-120

THROUGH: Antoine El-Hage, Ph.D., Chief  
Good Clinical Practice Branch II, HFD-47  
Division of Scientific Investigations

FROM: Constance Lewin, M.D.  
Good Clinical Practice Branch II, HFD-47  
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA: 21-231

APPLICANT: AstraZeneca Pharmaceuticals, L.P.

DRUG: \_\_\_\_\_ (zolmitriptan) Orally Disintegrating Tablets

CHEMICAL CLASSIFICATION: 3

THERAPEUTIC CLASSIFICATION: Standard Review

INDICATION: \_\_\_\_\_

ACTION GOAL DATE: February 14, 2001

## I. BACKGROUND:

Routine clinical inspections were conducted in support of the above-noted application and focused on protocol #311CIL/0107. This protocol was not conducted under a U. S. IND. Drs. Guy Boudreau, Jacques Meloche, and Marek Gawel were chosen for inspection. The data generated by these clinical investigators were determined to be critical to the approval process given that these investigators had enrolled a relatively large number of subjects. Goals of the inspections included validation of the primary efficacy endpoint data and subject safety parameters at the sites, along with an analysis of the adequacy of informed consent.

**II. RESULTS (by protocol/site):**

<b>NAME</b>	<b>LOCATION</b>	<b>ASSIGNED DATE</b>	<b>RECEIVED DATE</b>	<b>CLASSIFICATION</b>
Boudreau/ Meloche	Montreal, Quebec, Canada	July 27, 2000	November 24, 2000	NAI
Gawel	Toronto, Ontario, Canada	June 30, 2000	November 30, 2000	NAI

**Protocol #311CIL/0107**

**1. Site #1 (Guy Boudreau, M.D., and Jacques Meloche, M.D. – Montreal, Quebec, Canada):**

Twenty-six (26) subjects were enrolled, nineteen (19) of whom completed the study. Seven (7) subjects discontinued, for the following reasons: non-compliance (3), lost to follow-up (3), and consent withdrawal (1).

Records were reviewed for all enrolled subjects. No objectionable practices were noted; a Form FDA 483 was not issued.

Data acceptable

**2. Site #2 (Marek Gawel, M.D. – Toronto, Ontario, Canada):**

Twenty (20) subjects were enrolled, nineteen (19) of whom completed the study. One (1) subject discontinued due to non-compliance.

Records were reviewed for all enrolled subjects. No significant deviations from good clinical investigational practices or federal regulations were noted; a Form FDA 483 was not issued.

Data acceptable

**APPEARS THIS WAY  
ON ORIGINAL**

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

Drs. Boudreau, Meloche, and Gawel appear to have conducted protocol #311CIL/0107 in compliance with good clinical investigational practices and FDA regulations. It is therefore recommended that the data submitted by these clinical investigators may be used in support of pending NDA #21-231.

Key to Classification:

- NAI = No deviation from regulations. Data acceptable
- VAI = Minor deviation(s) from regulations. Data acceptable
- VAI-r = Deviation(s) from regulations, response requested. Data acceptable
- OAI = Significant deviations from regulations. Data unreliable

ISI 1/12/01  
Constance Lewin, M.D.  
Good Clinical Practice Branch II, HFD-47  
Division of Scientific Investigations

CONCURRENCE:

ISI 1/12/01  
Antoine El-Hage, Ph.D., Chief  
Good Clinical Practice Branch II  
Division of Scientific Investigations

DISTRIBUTION:

- NDA 20-231
- Division File
- HFD-45/Program Management Staff (electronic copy)
- HFD-47/Hajarian/Lewin
- HFD-47/GCP II Branch Chief
- HFD-47/Kline for GCPB File #####
- HFD-47/Reading File

APPEARS THIS WAY  
ON ORIGINAL

D

**THIS SECTION  
WAS  
DETERMINED  
NOT  
TO BE  
RELEASABLE**

(7)

D

**AstraZeneca Pharmaceuticals LP**  
**(zolmitriptan) Orally Disintegrating Tablets**

**PATENT INFORMATION ON ANY PATENT WHICH  
CLAIMS THE DRUG**

For further information regarding this section, please contact:

Judy W. Firor  
Regulatory Affairs Director  
(302) 886-7539  
AstraZeneca Pharmaceuticals LP  
1800 Concord Pike  
PO Box 15437  
Wilmington, DE 19850-5437

ZOMIG is a trademark, the property of the AstraZeneca Group.

AstraZeneca Pharmaceuticals LP  
1800 Concord Pike  
Wilmington, DE 19850-5437

(zolmitriptan) Orally Disintegrating Tablets  
NDA 21-231

Pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act, the information following below is made of record.

**A. PATENT INFORMATION ON ANY PATENT WHICH CLAIMS THE DRUG OR A METHOD OF USING THE DRUG.**

1. Active ingredients(s):

(S)-4-[[3-[2-(Dimethylamino)ethyl]-1H-indol-5-yl]methyl]-2-oxazolidinone.

2. Strength(s):

2.5 mg

3. Trade Name:

(zolmitriptan) Orally Disintegrating Tablets

4. Dosage Form, Route of Administration:

Tablet, Orally Disintegrating

5. Applicant Firm Name/Holder of the New Drug Application:

IPR Pharmaceuticals Inc.  
Carolina, Puerto Rico

US Agent:

AstraZeneca Pharmaceuticals LP  
1800 Concord Pike  
Wilmington, DE 19850-5437

6. NDA Number:

21-231

**APPEARS THIS WAY  
ON ORIGINAL**

**7. Approval Date (Original NDA 20-768):**

November 25, 1997

**8. Applicable Patents**

(i) US Patent No. 5,466,699

(a) Expiration Date:

November 14, 2012

(b) Type of Patent:

The patent claims the drug product as a compound per se, a method of using the compound, and a pharmaceutical composition containing the compound.

(c) Name of Patent Owner:

Zeneca Limited  
Macclesfield, Cheshire, England

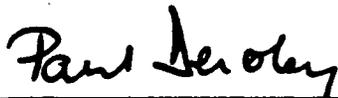
(d) Agent Authorized to Receive Notice:

The agent of the patent owner in the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the act and 21 CFR sections 314.52 and 314.95 is:

Cushman, Darby and Cushman,  
Intellectual Property Group of  
Pillsbury, Madison and Sutro, LLP  
1100 New York Avenue  
Washington, DC 2005-34918

(e) Original Declaration:

The undersigned declares that US Patent No. 5,466,699 covers the formulation, composition, and/or method of use of  (zolmitriptan) Orally Disintegrating Tablets. This product is the subject of this application for which approval is being sought.



---

PAUL M. DENERLEY, Ph.D.

## B. EXCLUSIVITY INFORMATION

### 1. Exclusivity Claim

AstraZeneca Pharmaceuticals LP claims an exclusivity period of three years for the change in  (zolmitriptan) Orally Disintegrating Tablets presented in this new drug application.

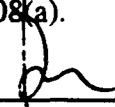
### 2. Authority for Exclusivity Claim

Exclusivity for the change in  (zolmitriptan) Orally Disintegrating Tablets presented in this supplemental new drug application is being claimed pursuant to 21 CFR Section 314.108(b)(4).

### 3. Information Demonstrating this New Drug Application Contains New Clinical Investigations Conducted or Sponsored by the Applicant that are Essential to the Approval of this New Drug Application.

#### a. Certification of New Clinical Investigations

AstraZeneca Pharmaceuticals LP certifies that to the best of its knowledge, each of the clinical investigations included in this new drug application meets the definition of "new clinical investigation" set forth in 21 CFR Section 314.108(a).

  
\_\_\_\_\_  
DAVID LEE, MD  
Medical Director

#### b. Essential to Approval

##### (i) Literature Search

Attached as Exhibit A is a list of all published studies and publicly available reports of clinical investigations known to AstraZeneca Pharmaceuticals LP through a literature search that are relevant to the conditions for which AstraZeneca Pharmaceuticals LP is seeking approval.

##### (ii) Certification

AstraZeneca Pharmaceuticals LP certifies that it has thoroughly searched the scientific literature and, to the best of its knowledge, the list of relevant published studies and/or publicly available reports is complete and accurate, and, in the opinion of AstraZeneca Pharmaceuticals LP, such published studies and/or publicly available reports do not provide a

sufficient basis for the approval of the conditions for which AstraZeneca Pharmaceuticals LP is seeking approval without reference to the new clinical investigation(s) in this supplemental new drug application.

  
\_\_\_\_\_  
DAVID LEE, MD  
Medical Director

(iii) Explanation

The published studies listed in Exhibit A do not provide sufficient basis for the approval of [REDACTED] (zolmitriptan) Orally Disintegrating Tablets because there is no previously available data on the clinical efficacy and tolerability on this formulation of [REDACTED]. Such information was requested by the Agency following a conference call with the Division of Neuropharmacological Drug Products on 10/12/1998 to discuss requirements for filing of the supplemental New Drug Application. The clinical studies submitted with this sNDA have defined the pharmacokinetic profile, clinical efficacy and tolerability of [REDACTED] in this new formulation that could not have been obtained from published information. These studies are therefore essential to the approval of this supplemental New Drug Application.

c. Conducted or Sponsored by the Applicant.

The new clinical investigations contained within this supplemental new drug application were conducted or sponsored by the applicant, IPR Pharmaceuticals Inc. Attached as Exhibit B is a statement from a certified public accountant which establishes that AstraZeneca UK Limited, the parent company of IPR Pharmaceuticals Inc., directly or through its predecessor in interest, Zeneca Limited, [REDACTED] for the conduct of these new clinical investigations.

**APPEARS THIS WAY  
ON ORIGINAL**

**EXHIBIT A**

**APPEARS THIS WAY  
ON ORIGINAL**

**Baker, D.E. New drugs approved by the FDA: New dosage forms and indications agents pending FDA approval: Major labeling changes. Hospital Pharmacy 2000, 35(1): 87-98**

**Tepper, S.J., Rapoport, A.M. The triptans: A summary. CNS Drugs 1999; 12(5): 403-417**

**PJB Publications Ltd. AstraZeneca's Zomig Rapimelt approved in ten countries. Scrip World Pharmaceutical News 1999; 2494: 22**

**PJB Publications Ltd. Battle of the triptans in the migraine market. Scrip World Pharmaceutical News 1998; 2369: 20.**

**PJB Publications Ltd. Maxalt in first European markets. Scrip World Pharmaceutical News 1998; 2356: 23.**

**PJB Publications Ltd. Merck & Co launches Maxalt in Canada. Scrip World Pharmaceutical News 1999; 2482: 21.**

**PJB Publications Ltd. Merck's Maxalt approved in Netherlands. Scrip World Pharmaceutical News 1998; 2313: 17.**

**PJB Publications Ltd. rizatriptan benzoate. Pharmaprojects**

**PJB Publications Ltd. The next wave of migraine drugs. Scrip World Pharmaceutical News 1997; 2243: 23.**

**PJB Publications Ltd. Zeneca files in Europe for fast-melt Zomig. Scrip World Pharmaceutical News 1999; 2414: 24**

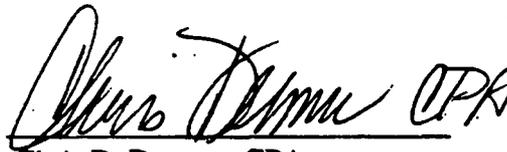
**PJB Publications Ltd. zolmitriptan. Pharmaprojects.**

**APPEARS THIS WAY  
ON ORIGINAL**

March 15, 2000

**AstraZeneca Pharmaceuticals LP**

This letter is to attest that for            (zolmitriptan) Orally Disintegrating Tablets, AstraZeneca UK Limited, the parent company of the applicant, IPR Pharmaceuticals Inc., directly or through its predecessor in interest, Zeneca Limited,                       for the conduct of the new clinical investigations included in this application.



Chris D. Degnan, CPA  
Director, R&D Finance  
Wilmington

CDD:lbt

**APPEARS THIS WAY  
ON ORIGINAL**



NDA 21-231

INFORMATION REQUEST LETTER

IPR Pharmaceuticals, Inc.  
US Agent—AstraZeneca Pharmaceuticals LP  
Attention: Judy W. Firor  
1800 Concord Pike, P. O. Box 8355  
Wilmington, DE 19803-8355

Dear Ms. Firor:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zomig ZMT (zolmitriptan) Orally Disintegrating Tablets.

We also refer to your submission dated May 26, 2000.

We are reviewing the Chemistry section of your submission and have the following comments and information requests. We need your prompt written response to continue our evaluation of your NDA.

- 1) Provide a letter of authorization from \_\_\_\_\_ allowing IPR or AstraZeneca to reference drug master file \_\_\_\_\_ for composition and control of Orange Flavor SN027512.
- 2) Your submission indicates that Orange Flavor SN027512 will be accepted based the supplier's certificate of analysis plus identity testing. Please clarify what tests will be accepted based on the supplier's certification and include appropriate acceptance criteria in the quality standard for this ingredient.
- 3) You state [Vol. 1.2, p. 21] that \_\_\_\_\_ orally disintegrating tablets are manufactured in a \_\_\_\_\_ . The process description submitted in your application does not provide any information regarding the \_\_\_\_\_ manufacture of this product. Additionally, the proposed master production and control record does not include any instruction regarding \_\_\_\_\_ during manufacture.
- 4) The process description should indicate the maximum time allowed for completion of tablet manufacture and packaging, and \_\_\_\_\_
- 5) The proposed master production and control record does not include a correction for the bulk drug substance assay. This is inconsistent with the approved manufacturing process for Zomig

Tablets under NDA 20-768 and procedures used to manufacture batches of the orally disintegrating tablet used in clinical trials in support of this application.

- 6) The proposed regulatory specification for zolmitriptan orally disintegrating tablets is not adequate. We note the following deficiencies in analytical procedures, acceptance criteria and supporting validation.

a) *Identification by IR*

Due to excipient interference, this test would not be considered a specific identity test. The analytical procedure, as written, is unclear and requires some additional validation data. Specifically, the instructions provided under "Interpretation" require that the sample spectrum correspond to that of the reference standard. The typical spectra provided in your submission would fail this test as written. Elsewhere in the procedure, you state that relative intensities may differ. The test instructions should be clarified and acceptance criteria should include specific to zolmitriptan that must correspond in sample and reference. Validation data showing absence of placebo interference at the selected wavelengths should be submitted.

We suggest that you investigate whether use of alternative sample preparation techniques would improve the specificity of this test.

b) *Assay*

Acceptance criteria for zolmitriptan should be stated as \_\_\_\_\_  
Test instructions state that quantitative composition of the solvent and flow rate may be adjusted. In the absence of supporting validation data, this instruction should be deleted. Alternatively, you may revise the test procedure to indicate validated ranges, with supporting data, within which these parameters may be adjusted.

c) *Related Substances*

Degradants that can routinely be observed in the product at significant levels, e.g., the \_\_\_\_\_ should be specified individually rather than as 'Individual other degradation products'. If the identity of a degradant is not known a suitable designation, such as \_\_\_\_\_, may be used in the product specification.

HPLC Methods 1 and 2 specify use of a zolmitriptan reference standard at 100% of nominal concentration to determine relatively low levels of impurities. Because of the potential for error in extrapolation, we recommend the use of a reference standard solution at a concentration similar to the expected analyte concentrations.

HPLC Methods 1 and 2 contain instructions for preparation and injection of a '0.05% w/w reporting level standard preparation'. Neither method includes criteria for determining if the method has the required degree of sensitivity. If the 0.05% standard solution is intended

to be part of the system suitability criteria, please clarify and include appropriate acceptance criteria.

The system suitability criteria for each related substance HPLC method should include a system suitability test for method precision at or near the working range for expected impurities. We suggest establishment of precision criteria ( \_\_\_\_\_ ) for \_\_\_\_\_ of nominal concentration.

For HPLC Method 2 ( \_\_\_\_\_ ) Clarify what the allowable pH range for the \_\_\_\_\_ is and provide validation data to demonstrate method ruggedness within this range. Test instructions state that quantitative composition of the solvent, flow rate and other non-critical instrument parameters may be adjusted. The test procedure should be revised to indicate validated ranges, with supporting data, within which these parameters may be adjusted. In the absence of such supporting validation data, the instruction should be deleted.

- 7) The immediate container label (blister foil) should be revised to include the recommended storage temperature. Use of the AstraZeneca name should be qualified by use of the phrase "manufactured for" (or "distributed by") and the corporate address should be included. Use of suitable abbreviations is acceptable.

If you have any questions, call Lana Chen, Pharm.D., Regulatory Management Officer, at (301) 594-2850.

Sincerely,

Maryla Guzewska, Ph.D.  
Chemistry Team Leader, Neurology Drugs for the  
Division of Neuropharmacological Drug Products,  
(HFD-120)  
DNDC I, Office of New Drug Chemistry  
Center for Drug Evaluation and Research

**APPEARS THIS WAY  
ON ORIGINAL**

/s/

-----  
Maryla Guzewska  
12/13/00 07:38:43 AM

**APPEARS THIS WAY  
ON ORIGINAL**

**AstraZeneca Pharmaceuticals LP**  
**(zolmitriptan) Orally Disintegrating Tablets**

**DEBARMENT CERTIFICATION**

For further information regarding this section, please contact:

Judy W. Firor  
Regulatory Affairs Director  
(302) 886-7539  
AstraZeneca Pharmaceuticals LP  
1800 Concord Pike  
PO Box 15437  
Wilmington, DE 19850-5437

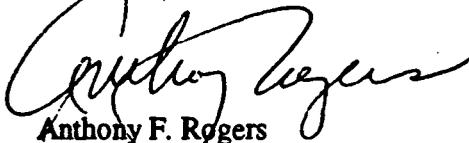
ZOMIG is a trademark, the property of the AstraZeneca Group.

APR 14 2000

Re:            (zolmitriptan) Orally Disintegrating Tablets  
NDA 21-231  
Debarment Certification

In response to the requirements of the Generic Drug Enforcement Act of 1992, I hereby certify on behalf of AstraZeneca Pharmaceuticals LP that we did not and will not use in connection with this application, the services of any person in any capacity debarred under section 306 (a) or (b).

Sincerely,



Anthony F. Rogers  
Vice President  
Regulatory Affairs Department  
(302) 886-2127  
(302) 886-2822 (fax)

AFR/PAD/jr

APPEARS THIS WAY  
ON ORIGINAL

# CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

ZOMIG 311CIL/0107

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	SEE ATTACHED REPORTS	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME John G. Goddard	TITLE Vice President, Finance & Chief Financial Officer
FIRM/ORGANIZATION AstraZeneca Pharmaceuticals	
SIGNATURE 	DATE March 1, 2000

### Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services  
Food and Drug Administration  
5600 Fishers Lane, Room 14C-03  
Rockville, MD 20857

c

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6 pages

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**AstraZeneca**  
US Regulatory Affairs

# FAX

Date: February 13, 2001

Number of pages including cover sheet: 1

Re: NDA 21-231 - (zolmitriptan) Orally Disintegrating Tablets

To: Ms. Lana Chen  
Division of Neuropharmaceutical Drug Products  
Center for Drug Evaluation and Research Food and Drug Administration  
HFD No. 120, Room No. 4031  
Woodmont Building II  
1451 Rockville Pike  
Rockville, MD 20852-1448

Fax: 301-594-2858  
From: Patricia A. DeFeo *PAO*  
Regulatory Project Manager,  
CNS

Phone: 302-886-2050  
Fax 302-886-2282  
phone: \_\_\_\_\_

Phone: 301-594-5529

**REMARKS:**  
 Urgent     For your review     Reply ASAP     Please comment

Attached please find the information you requested. A hard copy of this communication will follow shortly. Please do not hesitate to contact me with any questions or additional requests.

The information contained in this FAX is intended for the personal and confidential use of the designated recipient or recipients named above. If you are not the intended recipient or the person responsible for delivering it to the intended recipient or recipients, you are hereby notified that you have received this document in error, and that any reading, dissemination, distribution or copying of this document is strictly prohibited. If you have received this communication in error, please notify us immediately by FAX or telephone and return the original to us.



Russell G. Katz, MD  
 Division Director  
 Division of Neuropharmacological  
 Drug Products  
 Center for Drug Evaluation and Research  
 Food and Drug Administration  
 HFD No. 120, Room No. 4049  
 Woodmont Building II  
 1451 Rockville Pike  
 Rockville, MD 20852-1448

FEB 13 2001

Dear Dr. Katz:

Re: NDA 21-231  
 (zolmitriptan) Orally Disintegrating Tablets  
 Labeling Update for NDA 21-231

Reference is made to the facsimile received on February 12, 2001 by AstraZeneca Pharmaceuticals LP (AstraZeneca) from FDA requesting changes to the proposed labeling for (zolmitriptan) Orally Disintegrating Tablets NDA 21-231. Reference is also made to the telephone correspondence between FDA and AstraZeneca on the same day. AstraZeneca agrees to all of the requested labeling changes.

The confidentiality of this submission, and all information contained herein, is claimed by AstraZeneca under all applicable laws and regulations. Disclosure of any such information is not authorized without the prior written authorization of AstraZeneca.

Please direct any questions or comments for additional information to me, or in my absence, to Ms. Judy Firor at (302) 886-7539.

Sincerely,  
  
 Patricia A. DeFeo  
 Regulatory Project Manager, CNS  
 Regulatory Affairs  
 (302) 886-7539  
 (302) 886-2822 (fax)

JWF/DPC/mrsc  
 Enclosures

Desk Copy: Ms. Lana Chen, R.Ph., HFD No. 120, Room No. 4031

US Regulatory Affairs  
 AstraZeneca Pharmaceuticals LP  
 1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355