CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-959

PROPRIETARY NAME REVIEW(S)

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
WO 22, STOP: 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: March 2, 2006

NDA#: 21-959

NAME OF DRUG: Orapred ODT
(Prednisolone Sodium Phosphate Orally Disintegrating Tablets)
10 mg, 15 mg, and 30 mg (base)

NDA HOLDER: Medicis Pharmaceuticals

*** 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 Anesthesia, Analgesia, and Rheumatology Products (HFD-170), for assessment of the proprietary name, "Orapred ODT", regarding potential name confusion with other proprietary or established drug names. Draft container labels, carton and insert labeling were provided for review and comment at this time.

PRODUCT INFORMATION

Orapred ODT contains prednisolone sodium phosphate. Orapred ODT is indicated in the following conditions: (1) Allergic States, (2) Dermatologic Diseases, (3) Edematous States, (4) Endocrine Disorders, (5) Gastrointestinal Diseases, (6) Hematologic Disorders, (7) Neoplastic Diseases, (8) Nervous System, (9) Ophthalmic Diseases, (10) Respiratory Diseases, (11) Rheumatic Disorders, and (12) Miscellaneous Disorders. The sponsor also supplies Orapred as an oral solution. Orapred ODT may be substituted by Orapred solution, in any of the above indications at the same recommended dosages. Orapred solution should be used if the indicated dose cannot be obtained using Orapred ODT tablets. Doses of Orapred ODT range from 5 mg to 200 mg per day. Pediatric doses range from 0.14 mg/kg/day to 2 mg/kg/day, and 4 mg/m^2bsa/day to 60 mg/m^2bsa/day. The initial dosage should be maintained or adjusted until a satisfactory response is noted. The oral disintegrating tablet is packaged in a blister and should not be removed from the blister until just prior to dosing. Orapred ODT is an orally disintegrating tablet containing 10 mg, 15 mg, and 30 mg. It is available as a carton containing 48 tablets. Each carton contains eight cards of six tablets per card.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Orapred ODT 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[5]. The Saegis[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

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

1. DDMAC finds the proprietary name, Orapred ODT, acceptable from a promotional perspective.

2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Orapred ODT. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

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[1] MICROMEDEX Integrated Index, 2006, 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], Drugs@FDA, the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.
[4] Phonetic and orthographic Computer Analysis (POCA)
[5] WWW location http://www.uspto.gov/tmdb/index.html.
[6] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Orapred ODT 15mg #5  1 tab daily for 5 days Inpatient RX: Orapred oral 15mg 1 tab po QD x 5 days	Orapred ODT 15 mg dispense #5 Take one every day for five days.

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. DMETS notes that some of the study participants commented that "letters" used as part of the tradename should have a meaning or not be used. 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 Orapred ODT, the primary concerns related to look-alike and sound-alike confusion with Orapred and Orapred RT***. Safety concerns related to the 'ODT' modifier were also considered.

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

1. Look-alike and Sound-alike concerns:

Orapred ODT is the latest product extension to Orapred. Orapred is currently approved as an oral solution. There is also a pending application for Orapred RT*** which is an oral solution equivalent to Orapred Oral Solution but it does not need to be refrigerated. [redacted] this application is still pending and thus we must include this name for evaluation. Since all three products share the root name (Orapred), there was concern that confusion might occur between these products and the root name if the modifier was omitted. If the modifier for Orapred ODT was omitted, the patient would likely receive Orapred oral solution or Orapred RT***, once it is approved. Although both products contain the same ingredient, dose and frequency, the formulation may not be optimal for the patient's particular medical situation. Upon approval of Orapred ODT and Orapred RT***, multiple dosage forms of

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Orapred will be available. Once two different Orapred dosage forms (oral solution and orally disintegrating tablets) are marketed, practitioners will need to further clarify which dosage form will be appropriate for the individual patient prior to dispensing the drug. There will need to be an education campaign to alert health care practitioners to the new dosage forms including product differences.

2. Modifier (ODT) concerns:

DMETS evaluated the modifier 'ODT' for possible confusion among healthcare professionals. Currently, there are a number of products that employ a modifier in the proprietary name to identify an orally disintegrating product (see below). Although there is a theoretical potential for confusion among the modifiers of the currently marketed orally disintegrating tablets, we have not received any cases of confusion with these product names. Additionally, DMETS believes that it is unlikely that the root names of the drugs listed in Table 2 would be confused with the root name Orapred due to the different orthographic and phonologic presentation. However, upon approval of the product Orapred ODT, practitioners will still need to be educated with regards to the use of the appropriate modifier to decrease the potential for confusion with currently used modifiers and within the Orapred product line.

Table 2

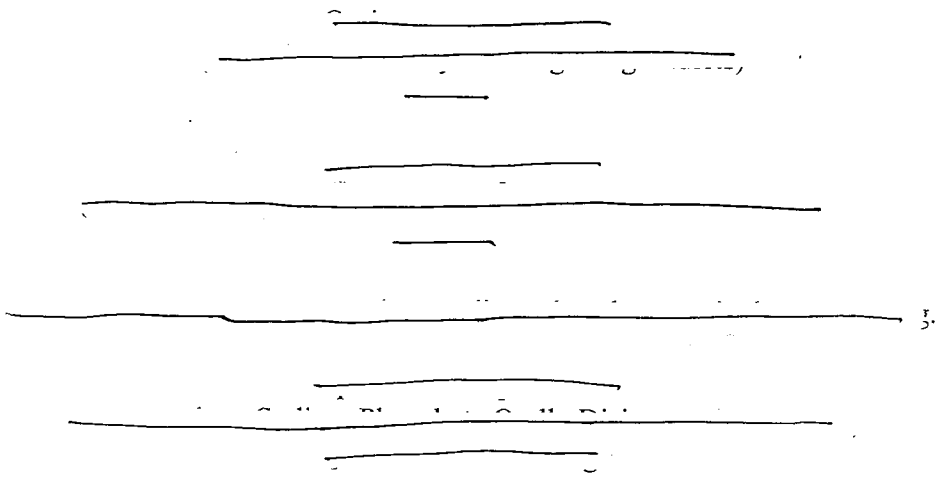
Modifiers for Orally Disintegrating Tablets	
Product Name	**Modifier**
Maxalt MLT	MLT (Melt)
Zofran ODT	ODT (Orally Disintegrating Tablets)
Fazaclo ODT	Clozapine (Orally Disintegrating Tablets)
Aricept ODT	Donepezil Hydrochloride (Orally Disintegrating Tablets)
Reglan ODT	Metoclopramide Hydrochloride (Orally Disintegrating Tablets)
[redacted]	[redacted]
Claritin Reditabs	Reditabs
Pepcid RPD	(RPD) No discernable meaning **
Remeron Soltab	Soltab
Zomig ZMT	(ZMT) No discernable meaning ***
Zyprexa Zydis	Zydis
* Proposed not FOI releasable. ** Per United States Patent and Trademark Office *** Per DMETS consult # 99-0109. Not FOI releasable.	

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container labels, carton and insert labeling of Orapred ODT, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. The strength of this product is based on the active moiety Prednisolone and not the salt Prednisolone Sodium Phosphate. In the current presentation, we note that the established name includes the salt and the Prednisolone equivalent are both presented on the label without clarification. We recommend revising the established name on the labels and labeling to one of the following examples:



Note: DMETS prefers the first example as an option because this nomenclature is consistent with USP recommendations on amount of ingredient per dosage unit.

2. The established name appears less than ½ the size of the proprietary name. Increase the prominence of the established name so that it is at least ½ the size of the proprietary name per 21 CFR201.10(g)(2). Similarly, increase the font size of the product strength so that it is more prominent and legible in comparison to the proprietary and established names.

3. Revise the proprietary name Orapred to appear in a straight line. The font used makes the name look handwritten and difficult to read. Additionally, if the Division allows the use of the modifier ODT, request the sponsor to revise the modifier color so that it is the same color as the root name, Orapred.

. Revise accordingly.

4. The display of grapes, outline of grapes, and colored 'waves' interfere with the readability of the proprietary and established names, as well as the strength. Additionally, the graphics are more prominent than the proprietary and established names and strength.

5. Ensure that the labels and labeling for Orapred ODT are distinct from Orapred and Orapred RT*** to decrease the potential for selection errors.

6. Add the statement "Do not break or use partial ODT tablets" to all labels and labeling. Additionally, if space permits, include the warning 'Do not remove the tablet from the blister until just prior to dosing'.

B. BLISTER LABEL

1. See GENERAL COMMENT A1, A2 and A6.

2. The blister label appears crowded. We recommend deleting the [redacted] statement to allow for more room. See comment A1.

3. Ensure the established name is ½ the size of the proprietary name and the prominence of the strengths is commensurate with that of the established name.

4. Include directions for removal of the tablet from the blister pack, (e.g. peel, etc.) to prevent patients from pushing the tablet through the blister.

5. The layout and colors used to designate the 10 mg, 15 mg, and 30 mg are identical. [redacted]

C. CARTON LABELING

1. See GENERAL COMMENTS.

2. The established name and strength are separated by a purple line. Delete the line as there should be no intervening matter between the drug name and strength.

3. Revise net quantity to read '[redacted],' which accurately reflects the composition of the cards.

D. INSERT LABELING

1. Revise the statement in the HOW SUPPLIED section from '[redacted];' to '8 cards containing 6 tablets'.

2. The PRECAUTIONS and DOSAGE and ADMINISTRATION sections contain the statement 'Do not break or use partial ODT tablets'. We recommend that this information be bolded to provide greater prominence in order to reflect the importance of this information.

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Appendix A:

Verbal	Inpatient Written	Outpatient Written
Orapred ODT	Orapred ODT	Orapred ODT
Orapred ODT	Alapred OPT	Orapred ODT
Orapred ODT	Mapeed OPT	Orapred ODT
Orapred ODT	Oraped ODT	Orapred ODT
Orapred ODT	Orapeed OPT	Orapred ODT
Orapred ODT	Orapred ODT	Otiapred
Orapred ODT	Orapred ODT	Otiapred ODT
Orapred ODT	Orapred ODT	Otinpred ODT
Orapred ODT	Orapred ODT	Otraphed ODT
	Orapred ODT	Otrapred ODT
	Orapred ODT	Otrapred ODT
	Orapred OPT	
	Orapred OPT	
	vespeed opt	

Comment from study participants:

- Orapred ODT (Comment: Letters should have meaning or not be used)

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

/s/

Linda Wisniewski
4/12/2006 07:53:49 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
4/12/2006 08:44:23 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
4/12/2006 11:39:47 AM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, Director DMETS in her absence