CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-067

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; White Oak 22; Mail Stop 4447)

DATE RECEIVED: 12/1/06 **DATE OF DOCUMENT:** 11/22/06	**DESIRED COMPLETION DATE:** 2/22/07 **PDUFA DATE:** 6/14/07	**OSE REVIEW #:** 2006-926

TO: Bob Rappaport, MD
Director, Division of Analgesics, Anesthetics and Rheumatology Products
HFD-170

THROUGH: Nora Roselle, PharmD, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Felicia Duffy, RN, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME: **Flo-Pred** (Prednisolone) Oral Suspension 5 mg/5 mL and 15 mg/5 mL **)A #:** 22-067	**SPONSOR:** Taro Pharmaceuticals

RECOMMENDATIONS:

1. DMETS has no objection to the use of the proprietary name, Flo-Pred. 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 approvals of other proprietary or established names from the signature date of this document.

2. DMETS anticipates selection errors between the 5 mg/5 mL and 15 mg/5 mL strengths. Thus, we recommend implementation of the label and labeling revisions outlined in section III of this review in order to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name, Flo-Pred, acceptable from a promotional perspective.

4. We recommend consulting Richard Lostritto, Chair of the CDER Labeling and Nomenclature committee for the proper designation of the established name.

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 Nancy Clark, Project Manager, at 301-796-1187.

Division of Medication Errors and Technical Support
Office of Surveillance and Epidemiology
HFD-420; WO22; Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: January 24, 2007

NDA #: 22-067

NAME OF DRUG: **Flo-Pred**
(Prednisolone) Oral Suspension
5 mg/5 mL and 15 mg/5 mL

NDA SPONSOR: Taro Pharmaceuticals

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I. INTRODUCTION

This consult was written in response to a request from the Division of Analgesics, Anesthetics and Rheumatology Products, for an assessment of the proprietary name "Flo-Pred", regarding potential name confusion with other proprietary or established drug names. Container labels, carton and package insert labeling were provided for review and comment.

The sponsor previously submitted the proprietary names [redacted] The Division of Drug Marketing, Advertising and Communications (DDMAC) found both names unacceptable due to [redacted] The Division agreed with DDMAC's objection, therefore, DMETS did not conduct a safety review of the proprietary names, [redacted] Thus, the sponsor submitted Flo-Pred and [redacted] as alternate proprietary names. b(4)

PRODUCT INFORMATION

Flo-Pred (prednisolone oral suspension) is an anti-inflammatory drug indicated for the treatment of the following conditions: endocrine disorders, as adjunctive therapy for short-term administration in rheumatic disorders, [redacted] dermatologic diseases, severe and acute chronic allergic and inflammatory processes involving the eye, respiratory diseases, hematologic diseases, for palliative management of certain neoplastic diseases, [redacted] and to tide the patient over a critical period of certain gastrointestinal diseases. The initial dosage of prednisolone may range from 5 mg to 60 mg per day, depending upon the specific disease being treated. Dosages should be individualized according to the severity of the disease and the response of the patient. Flo-Pred will be available as a cherry flavored oral suspension in two concentrations: 5 mg/5 mL and 15 mg/5 mL. Both concentrations will be dispensed in 120 mL [redacted] bottles. b(4)

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of the internet, 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 Flo-Pred 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. Following completion of these initial steps, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly, integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Flo-Pred. 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, Flo-Pred, acceptable from a promotional perspective.

2. The Expert Panel identified fourteen proprietary names that were thought to have potential for confusion with Flo-Pred. The names are as follows: Fluxid, Florinef, Flonase, Floropryl, Flagyl, Flo-Pack, Levophed, Poly-Pred, AK-Pred, Flovent, Floxin, Flolan, Orapred, and Lopid. Upon independent review, one additional name, Slo-Bid, was identified as a name that may potentially be confused with Flo-Pred.

   Of these fifteen names, the following eleven names, Florinef, Flonase, Floropryl, Flagyl, Flolan, Floxin, Levophed, Poly-Pred, AK-Pred, Slo-Bid, and Flo-Pack, were not reviewed further due to the lack of significant look-alike similarities, sound-alike similarities, and/or differentiating product characteristics to Flo-Pred which may include the following: indication for use, product strength, usual dosage, route of administration, frequency of administration, dosage form, prescriber population, patient population, area of specialty use (e.g., OR, specialty clinic), storage conditions, product unavailability, and/or area of marketing. Although Flo-Pack and Flo-Pred share some orthographic similarities, Flo-Pack is a packaging configuration used with the drug Anectine, thus it is ordered as Anectine Flo-

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[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, 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 98-07, 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

Pack. Anectine Flo-Pack is a powder for infusion in which Flo-Pack would not be written by itself.

The remaining product characteristics of the proprietary names to be reviewed are listed in Table 1 (see page below), along with the dosage forms available and usual dosage.

3. A member of the Expert Panel also indicated that "Flo" sounds like it has something to do with "flow". Additionally, a Panel member indicated that Flo-Pred sounds like an inhaler device.

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

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other**
Flo-Pred	Prednisolone Oral Suspension: 5 mg/5 mL and 15 mg/5 mL	Initial doses may vary from 5 mg to 60 mg per day. Dosage is individualized according to the severity of the disease and the response of the patient.	
Fluxid	Famotidine Orally Disintegrating Tablets: 20 mg and 40 mg	Duodenal ulcer: 20 mg to 40 mg po QD or 20 mg po BID. Benign gastric ulcer: 40 mg po QHS. GERD: 20 mg po BID for up to 6 weeks or 20 mg to 40 mg po BID for up to 12 weeks. Hypersecretory conditions: 20 mg to 160 mg po Q6 hrs. Pediatric patients 6-16 year old: 1 mg/kg/day po BID up to 40 mg BID.	LA
Flomax	Tamsulosin HCl Capsules: 0.4 mg	0.4 mg to 0.8 mg po QD.	LA
Orapred Orapred ODT	Prednisolone Sodium Phosphate Oral Solution: 15 mg/5 mL Orally Disintegrating Tablets: 10 mg, 15 mg, and 30 mg	Initial dose may vary from 5 mg to 60 mg per day, depending upon the disease being treated. Dosages should be individualized on the bases of the disease and patient response.	LA
Lopid	Gemfibrozil Tablets: 600 mg	600 mg po BID 30 minutes before the morning and evening meal.	LA/SA

*Frequently used, not all-inclusive.
**LA (look-alike), SA (sound-alike)

B. 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 Flo-Pred 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 124 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and an outpatient order were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Flo-Pred (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Inpatient sample: Flopred Give 1 teaspoonful by mouth once a day Outpatient sample: Flo-pred #120ml Give 1 tsp po qd	Flo-Pred #120 mL Give 1 tsp by mouth once a day

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.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name "Flo-Pred", DMETS acknowledges that the Sponsor includes a hyphen in the proprietary name, Flo-Pred. However, we note that in the practical setting, the proprietary name may or may not be written with a hyphen, as noted in the verbal prescription studies. Thus, we will evaluate the name both with and without the hyphen.

The primary concerns relating to look-alike and/or sound-alike confusion with Flo-Pred are Fluxid, Flomax, Orapred, and Lopid. Additionally, there was some concern that "Flo" could mean "flow" and the name "Flo-Pred" sounds like an inhaler device. DMETS also had concerns with the design of the enclosed measuring teaspoon. These concerns are addressed and recommendations are provided to improve the safe use of the measuring teaspoon in section IIID of this review.

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, Flo-Pred.

DMETS acknowledges the comments from the EPD discussion in which the Panel mentioned that "Flo" sounds like "flow" and that "Flo-Pred" sounds like an inhalation device. In review of these comments, we determined that "Flo" has been used with other drug products that are not pulmonary agents and thus this would not represent a safety hazard. Another comment made by the Expert Panel concerned the association of Flo-Pred as an inhalation device. There are products that contain "flo" in the name that are not oral inhalers such as Flolan, Flonase, and Flomax. Additionally, DDMAC was not concerned with this name, and thus, DMETS does not believe this is a safety issue.

Additionally, since prednisolone has been marketed as a syrup and oral suspension in both the 5 mg/5 mL and 15 mg/5 mL concentrations, DMETS conducted a search of the Adverse Event Reporting System to identify confusion between the concentrations. The MedDRA Preferred Terms (PT) "Underdose", "Incorrect Dose Administered", "Wrong Drug Administered", "Drug

Administration Error", "Intercepted Drug Administration", "Overdose", "Accidental Overdose", "Intercepted Medication Error", "Circumstance or Information Capable of Leading to Medication Error", "Medication Error", "Drug Dispensing Error", "Intercepted Drug Dispensing Error", "Pharmaceutical Product Complaint" and the active ingredients "Prednisolone" and "Prednisolone Sodium Phosphate" were used a search criteria. DMETS retrieved one medication error related an error between the 5 mg/5 mL and 15 mg/5 mL strengths. This report occurred in 1999, and the patient experienced facial and body skin discoloration in addition to an unusual temperament.

DMETS requested data from MEDMARX** in reference to medication errors between the 5 mg/5 mL and 15 mg/5 mL strengths of prednisolone.

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The patient outcome was not indicated in any of the reports. We anticipate similar errors with this product due to selection errors between these strengths. We have addressed these concerns in the labeling, packaging and safety section (section III) of this review.

DMETS has the following comments in review of the names identified with potential look- alike and/or sound-alike similarities with Flo-Pred.

1. Fluxid was identified as a name with similar appearance to Flo-Pred. Fluxid is an orally disintegrating tablet that contains famotidine. It was approved in September 2004 for the short-term treatment of active duodenal ulcer, benign gastric ulcer, GERD, esophagitis due to GERD, and hypersecretory conditions. The product is currently not marketed by its Sponsor; however, the NDA remains active. Fluxid is available in 20 mg and 40 mg orally disintegrating tablets and may be dosed from 20 mg to 40 mg by mouth once daily or twice daily.

   Fluxid and Flo-Pred may appear similar as the "Flu" in Fluxid and the "Flo" in Flo-Pred can look similar when scripted if the hyphen is omitted from Flo-Pred. However, in combination, the endings look different ("xid" vs. "pred").

   Fluxid
   Flopred

   Although Fluxid and Flo-Pred will be available in different dosage forms (orally disintegrating tablets vs. oral suspension), both products are administered orally and may overlap in frequency of administration (QD or BID). Despite the different product strengths (20 mg and 40 mg vs. 5 mg/5 mL and 15 mg/5 mL), Fluxid and Flo-Pred may share overlapping doses (20 mg to 60 mg).

   Prescriptions for Flo-Pred will most likely indicate the product strength and the volume/dose to be administered (e.g., Flo-Pred 15 mg/5 mL, give 1 teaspoon by mouth once daily) especially since Flo-Pred will be available in two strengths. In this case, the dosing instructions, which will indicate a volume (e.g. ½ teaspoon, 1 teaspoon, 5 mL), will help to differentiate Flo-Pred from

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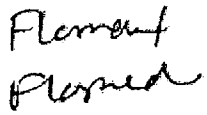
Fluxid. Therefore, DMETS believes the product strength, the dosing instructions, and the lack of strong look-alike similarity will minimize the potential for confusion between Fluxid and Flo-Pred.

2. Flomax was identified as a name with similar appearance to Flo-Pred when scripted. Flomax contains tamsulosin hydrochloride and is indicated for the treatment of benign prostatic hyperplasia. Flomax is dosed at 0.4 mg to 0.8 mg once daily and is available in 0.4 mg capsules.

   Flomax and Flo-Pred share the same beginning (Flo). The letters "pr" in Flo-Pred may resemble the letter "m" in Flomax when scripted (see below). Additionally, the letters "a" and "e" may also appear similar when scripted. However, when combined together the ending of the names ("max" vs. "pred") look different and help differentiate the names.

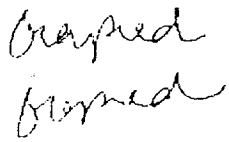


   Flomax and Flo-Pred may overlap in frequency of administration (QD). Although each drug will be available in different dosage forms (capsules vs. oral suspension), both drugs are administered orally. Despite these similarities, Flomax and Flo-Pred differ in strength (0.4 mg vs. 5 mg/5 mL and 15 mg/5 mL), and usual dose (0.4 mg or 0.8 mg or 1- 2 capsules vs. 5 mg to 60 mg or number of teaspoons). Prescriptions for Flo-Pred will most likely be prescribed with the strength specified and the volume/dose to be administered (e.g., Flo-Pred 5 mg/5 mL, give 1 teaspoonful by mouth once daily). In this case, the specification of the product strength and directions for use will help to differentiate Flo-Pred from Flomax.

   Although Flomax and Flo-Pred share some orthographic similarities, the products will be differentiated by their strength and dose. Therefore, the concern of confusion between Flomax and Flo-Pred is minimal.

3. Orapred was identified as a name with similar appearance to the proposed name, Flo-Pred, if it is written without a hyphen. Orapred contains prednisolone sodium phosphate, and is indicated to treat various conditions such as endocrine disorders, rheumatic disorders, dermatologic diseases, allergic states, ophthalmic diseases, respiratory diseases, hematologic disorders, neoplastic diseases, edematous states, gastrointestinal diseases, acute exacerbations of multiple sclerosis and other miscellaneous diseases and disorders. Orapred is available as an orally disintegrating tablet in 10 mg, 20 mg, and 30 mg. It is also available as a 15 mg/5 mL oral solution.

   Orapred and Flo-Pred both contain 7 letters. The beginning of Orapred and Flo-Pred (Ora vs. Flo) may look similar if the "f" is scripted in lowercase, and the upstroke of the "f" is not prominent. The letters "ra" and the "lo" may also resemble one other when scripted (see below). Both names also share the same ending (pred).



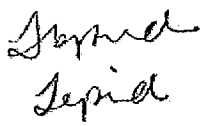
   Orapred and Flo-Pred share several overlapping product characteristics which includes: active ingredient (prednisolone), indication (various conditions), product strength (15 mg/5 mL), route of administration (oral), dosage form (oral solution/oral suspension), usual dose (5 mg to 60 mg), and frequency of administration (may vary). Since Orapred is available in only one strength, a prescriber would not necessarily have to specify the product strength. Thus, if a

prescription for: Orapred, take 1 teaspoonful po QD, #120, is correctly interpreted as Orapred, then the patient would receive the correct product and dose. If the same prescription is misinterpreted as Flo-Pred, then a pharmacist would need to clarify the product strength in order to ensure the patient receives the appropriate drug and dose. Furthermore, if the same prescription is misinterpreted as Orapred, then there will be no harm as both products are clinically interchangeable per discussion with the Division Medical Officer.

Although Orapred and Flo-Pred may appear almost identical, and they share numerous product characteristics, the product strength is the differentiating product characteristic that will help to distinguish the two products. Therefore, we believe Orapred and Flo-Pred may co-exist in the marketplace.

4. Lopid was identified as a name with similar appearance and sound to Flo-Pred. Lopid contains gemfibrozil and is indicated for the treatment of hypertriglyceridemia and for the prevention of cardiovascular disease. Lopid is available as a 600 mg tablet, and is dosed as 600 mg twice daily.

   Lopid and Flo-Pred may appear similar because the "F" and "L" may look similar when scripted. The letters "pid" and "pred" may also share some resemblance when scripted (see below). However, the upstroke of the letter "l" in Flo-Pred and the letter "r" in Flo-Pred helps to lengthen the name and differentiate it from Lopid.



   Flo-Pred is phonetically similar to Lopid because the "L" in Flo-Pred is prominent in sound, and Flo-Pred over the phone may be misinterpreted as "Lopred", which is almost identical to Lopid.

   Lopid and Flo-Pred may share an overlapping frequency of administration (BID). Although Lopid and Flo-Pred differ in dosage form (tablets vs. oral suspension), both are administered orally. Conversely, Lopid and Flo-Pred differ in strength (600 mg vs. 5 mg/5 mL and 15 mg/5 mL), and usual dose (1200 mg or 2 tablets vs. 5 mg to 60 mg or number of teaspoons). Furthermore, dosing instructions for Flo-pred will help to differentiate it from Lopid because it will contain a volume (e.g., ½ teaspoon, 1 teaspoon) whereas Lopid will be dosed in the number of tablets (e.g., take 2 tablets). Therefore, DMETS believes the product strength and dosing instructions will minimize confusion between Lopid and Flo-Pred.

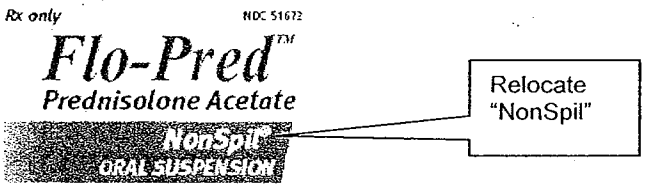
III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In review of the container labels, carton and insert labeling of Flo-Pred, DMETS has focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, which may minimize potential user error.

A. GENERAL COMMENTS

1. The chemical name for Flo-Pred is described as prednisolone throughout the package insert; however, it is described as prednisolone acetate on the carton and container labels. The labels and labeling should be consistent. Because the dosing of Flo-Pred is based on the active moiety rather than the salt, we recommend using prednisolone rather than prednisolone acetate. DMETS recommends that the Division consult Richard Lostritto, Chair of the CDER Labeling and Nomenclature Committee (LNC), Karl Stiller (the Project Manager Assigned to LNC), and the assigned Office of New Drugs Quality Assessment (ONDQA) chemist regarding the appropriate designation of the established name.

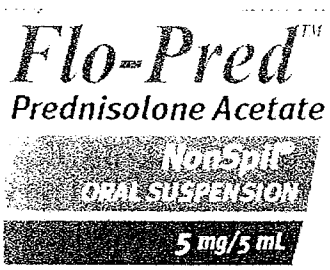
2. The Sponsor utilizes the word "NonSpil" in the carton and container labeling. However, the placement of this term makes "NonSpil" appear as though it is part of the established name. Since "NonSpil" is a form of technology, this statement should be relocated so it does not separate the finished dosage form from the active ingredient. We also recommend not highlighting these statements. Highlighting these statements makes the 5 mg and 15 mg bottle similar in appearance. We anticipate selection errors between these products because the strengths are similar and we have had post-marketing errors with these strengths. Thus, making the bottles look similar will increase this risk of these selection errors.

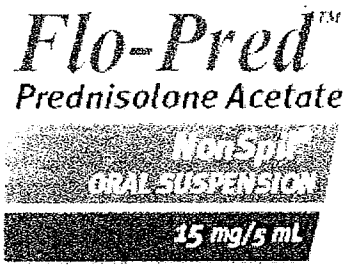


3. The dosage form (oral suspension) does not appear in conjunction with the active moiety. Since the dosage form is part of the established name, it should appear in close proximity to prednisolone acetate. We recommend relocating "oral suspension" in the light blue highlighted box to appear in close proximity to the established name, and delete the light blue box. The established name should read as:

   Prednisolone Oral Suspension *or* (Prednisolone) Oral Suspension

4. The dark blue box that highlights the 5 mg/5 mL strength, and the purple box that highlights the 15 mg/ 5 mL strength are similar in appearance (see below). The similarity in appearance may lead to selection errors. Thus, revise the color of the highlighted boxes in order to clearly differentiate the strengths from one another which may be helpful to prevent selection errors.



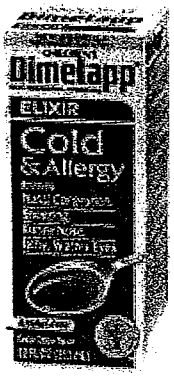


5. The product strength appears small and is far away from the established name. In order to improve readability, increase the size of the product strength and relocate the product strength to immediately follow the established name and dosage form.

6. We note the "Rx Only" statement appears in red font. The red font makes this statement stand out above all other text. Red font is typically used to highlight important information or warning information. Thus, to decrease the prominence of this statement, revise it so that this statement is not in red.

7. The carton labeling contains a picture of a spoon containing medication with the caption "Spill Resistant" beneath the picture. This picture is distracting on the carton labeling. Additionally, the picture may lead consumers to believe that Flo-Pred is an OTC product, as some OTC products have used this type of picture on their labels (see comparison on page 10). We find this type of picture on a prescription product to be promotional and unless this picture is a true representation of the teaspoon provided in the carton, then this is misleading and we recommend deleting this graphic representation from the labeling.

Flo-Pred



OTC Product

8. The color of the oral suspension on the carton appears red. However, there is no description of the color of the drug product in the package insert. Although the package insert states that Flo-Pred is cherry flavored, this does not necessarily mean that the drug product is red in color. There is no indication in the Description section of the PI of that described the color of the drug or that a color is listed as an inactive ingredient. It can be confusing if the drug product appears red on the carton, but in actuality, the product is colorless or is any other color than what is depicted on the labeling. Thus, we recommend removing the teaspoon from the carton labeling, and include a description of the color of the drug product in the package insert.

9. The Sponsor intends to market both strengths of Flo-Pred in 120 mL [redacted] bottles. The overlap in packaging size and presentation may increase the potential for shelf selection errors. Thus, we recommend packaging the different strengths in non-overlapping bottle sizes to minimize the potential for selection errors. b(4)

10. The packaging for the 5 mg/5 mL and 15 mg/5 mL bottles appear as though they should be dispensed as a unit-of-use because one spoon is included in the carton with the drug product. The container includes more drug than what would be required. Because of this, the contents will likely be transferred into a separate amber pharmacy bottle. If these are considered to be unit-of-use bottles, then we recommend that the bottles contain no more than the maximum dose for the drug product. Otherwise, the spoon should not be included in this package.

B. CONTAINER LABELS

1. Physicians Sample (1 oz bottles- 5 mg/5 mL and 15 mg/5 mL)

   a. See General Comments A1 though A5.

   b. The Sponsor's name appears as prominent as the product name, and is more prominent than the product strength. Therefore, decrease the prominence of the Sponsor's name.

   c. The "Physicians Sample Only" statement is small and difficult to see on the labeling. Increase the prominence of this statement and relocate it above the proprietary name. Additionally, revise the statement so it reads as: "Physicians Sample Only-Not for Sale".

   d. Relocate the statement "Keep this and all medications out of the reach of children" to the back panel.

   e. Ensure the physician sample bottles have child-resistant caps in compliance with the Poison Prevention Act.

f. Include a statement that instructs the patient to use the teaspoon provided as noted on the commercial container labels.

b(4)

2. 4 oz [redacted] bottles (5 mg/5mL and 15 mg/5 mL)

a. See General Comments A1 through A5.

b. See comments B1b and B1d.

C. CARTON LABELING

1. Physician Display Carton (1 oz bottles- 5 mg/5 mL and 15 mg/5 mL)

a. See General Comments A1 through A6.

b. The "Physician Sample Only-Not for Sale" statement does not appear on the physician display carton. Add this statement to the primary display carton for completeness.

c. Email correspondence with the sponsor confirmed that a calibrated teaspoon will be included in with the physician samples. However, it is not clear if only 1 spoon will be provided for the entire carton, or if enough spoons will be provided for each 1 ounce sample. Please clarify. Additionally, the statement "Attention: use this product only with the enclosed teaspoon...." does not appear on the physician display carton. Include this statement on the physician sample cartons and instruct practitioners to dispense a spoon with each sample.

2. 4 oz [redacted] bottles (5 mg/5mL and 15 mg/5 mL) b(4)

a. See General Comments A1 through A6.

b. The statement on the side panel that indicates the product should only be used with the enclosed teaspoon should be relocated to the primary display panel, as this is important information. Increase the prominence of this statement as many consumers are accustomed to administering liquids with a teaspoon from their kitchen.

D. PACKAGE INSERT LABELING

[redacted] b(4)

[redacted] This information conflicts with the statement on the carton labeling that indicates that the drug product has a teaspoon enclosed in the carton. If the Sponsor intends to include a calibrated measuring device with Flo-Pred, it should be accurately reflected in the "How Supplied" section, rather than mentioned in a statement to the pharmacist.

E. TEASPOON

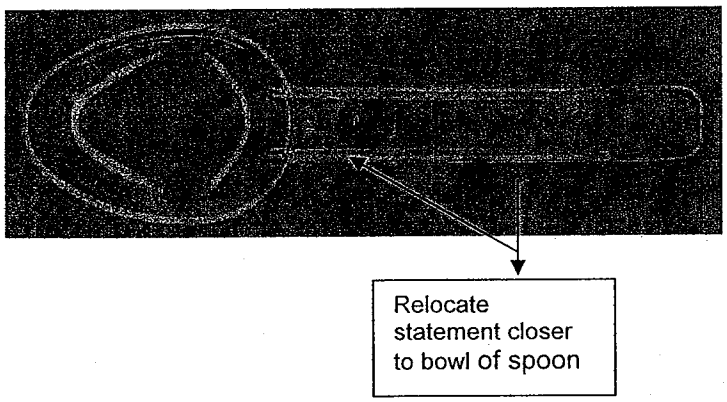
1. We note the teaspoon enclosed in the carton is not an optimal design and may contribute to error. The depth of the spoon and width of the spoon may be difficult for some patients to use, especially small children. We strongly recommend the sponsor consider an oral dosing syringe as the delivery device for this drug product. If the Sponsor intends to use the teaspoon provided, we have the following comments:

a. The embossed print on the teaspoon provided in the carton is nearly impossible to read because it is the same transparent color as the teaspoon. We recommend using

contrasting color for the embossed print, which includes the wording and the ½ teaspoon line, in order to improve readability.

b. We recommend revising "½ teaspoon to line" to read as "½ teaspoon to this line" so that t user does not fill the entire teaspoon for the ½ teaspoon dose.

c. Revise the statement "1 tsp=5 mL when full" to "1 tsp (5 mL) when spoon is full" and relocate this statement closer to the bowl of the spoon so that the user's fingers are less likely to cover this information.



d. In reference to the commercially available sizes of 120 mL [redacted] DMETS questions b(4) where pharmacists or patients will get a teaspoon if a practitioner orders 90 mL and the spoon is not in the carton because it has been dispensed with a separate prescription. This is likely to occur in situations where pediatric patients receive a burst of 5-7 days of this product. Please comment.

Appendix A

Flo-Pred prescription study results

Written Inpatient	Written Outpatient	Verbal
flaned	Flo-Phed	Flopred
Flaped	Flo-Pred	Flopred
Flaped	Flo-pred	Flopred
Flaped	Flo-pred	Flopred
Flaped	Flo-Pred	Flopred
Flaped	Flo-pred	Flopred
Flaped	Flo-pred	Flopred
Flaped	Flo-Pred	
Flapred	Flo-Pred	
Flayred	Flo-Pred	
Floped	Flo-Pred	
Floped	Flo-pred	
Haped	Flo-pred	
Haped		
Haped		
Hoped		

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/s/

Felicia Duffy
4/17/2007 12:06:15 PM
DRUG SAFETY OFFICE REVIEWER

Nora L. Roselle
4/17/2007 12:14:31 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
4/17/2007 12:28:28 PM
DRUG SAFETY OFFICE REVIEWER