CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-959

CHEMISTRY REVIEW(S)

NDA 21-959

Orapred ODT™ (prednisolone sodium phosphate orally disintegrating tablets) equivalent to prednisolone 10 mg, 15 mg, and 30 mg

Medicis Pediatrics, Inc.

Rao Puttagunta, Ph.D.
Branch III/Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Reviewed for
The Division of Analgesia, Anesthesia, and Rheumatology Products (DAARP), HFD-170

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Chemistry Review Data Sheet

1. NDA #: 21-959

2. REVIEW #: 1

3. REVIEW DATE: 11-MAY-2006

4. REVIEWER: Rao Puttagunta

5. PREVIOUS DOCUMENTS: N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	28-JUL-2005
Amendment (BC)	06-APR-2006
Amendment (BC)	25-APR-2006
Amendment (BL)	12-MAY-2006
Amendment (BC)	23-MAY-2006

7. NAME & ADDRESS OF APPLICANT:

Name: Medicis Pediatrics, Inc.
(A wholly owned subsidiary of Meidcis Pharmcetical Corp.)
Address: 8125 N. Hayden Road
Scottsdale, AZ 85258

Representative: Ruhee Ahmed, Ph.D.
Manager, Regulatory Affairs
Biomarin Pharmaceutical Inc. (Authorized US agent)
105 Digital Drive, Novato, CA 94949
Telephone: 415-506-6735

8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: Orapred ODT™
   b) Non-Proprietary Name (USAN): Prednisolone Sodium Phosphate Orally Disintegrating Tablets
   c) Code Name/# (ONDC only): N/A
   d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(2)

RLD: Pediapred® (prednisolone sodium phosphate) Oral Solution, 5 mg base/5 mL, Celltech Pharmaceuticals, Inc., NDA 19-157

10. PHARMACOL. CATEGORY: Glucocorticoid

11. DOSAGE FORM: Orally Disintegrating Tablet

12. STRENGTH/POTENCY: 10 mg, 15 mg, and 30 mg prednisolone base/tablet

13. ROUTE OF ADMINISTRATION: Oral

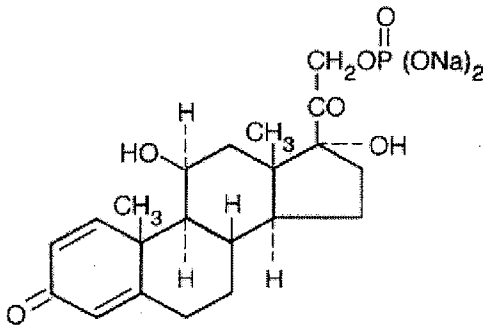
14. Rx/OTC DISPENSED: __X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Chemical Name: Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-(phosphonooxy)-, disodium salt, (11β)-;

Molecular Formula: $C_{21}H_{27}Na_2O_8P$ **Molecular Weight:** 484.39

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	[redacted]	3	Adequate	7/07/05 (R.S. Randad)	---
[redacted]	III	[redacted]	[redacted]	1	Adequate	5/11/06 (R. Puttagunta)	---
[redacted]	IV	[redacted]	[redacted]	7	N/A	---	CFR & FEMA compliance

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
PIND	70,495	Orapred™ ODT (prednisolone sodium phosphate)

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	4/10/06	
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	Disintegration time	5/22/06	Guirag Poochikian
Methods Validation	N/A per new ONDC policy		
DMETS	Acceptable	4/12/06	Linda Wisniewski
DDMAC	Acceptable	5/03/05	Michelle Safarik
EA	Categorical Exclusion		Rao Puttagunta
Microbiology	N/A		

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes ____ No If no, explain reason(s) below:

APPEARS THIS WAY
ON ORIGINAL

The Chemistry Review for NDA 21-959

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the CMC standpoint this NDA is recommended for approval.

An expiration dating period of 24 months may be granted.

The applicant was asked to clarify whether the barcode on the blister contains the NDC number and any additional information. The applicant can comply with the bar code rule within 60 days of approval. This should be included in the action letter.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

1. Drug Substance

Prednisolone sodium phosphate is manufactured by [redacted]
The CMC information on prednisolone sodium phosphate (PSP) was referenced to DMF [redacted]. The DMF has been recently reviewed and found to be adequate.

2. Drug Product:

The Orapred ODT (prednisolone sodium phosphate) orally disintegrating tablets contain 13.4 mg, 20.2 mg or 40.3 mg of prednisolone sodium phosphate (equivalent to 10 mg, 15 mg, or 30 mg of prednisolone respectively) per tablet. The orally disintegrating tablets were formulated with [redacted]. The [redacted] The reference listed drug Pediapred® (prednisolone sodium phosphate) Oral Solution contains 5 mg of prednisolone/5 mL.

The drug product is packaged in unit dose blisters.

B. Description of How the Drug Product is Intended to be Used

The Orapred ODT tablets are used for the same multiple indications as other glucocorticoid preparations, such as Orapred® or Pediapred®. Orapred ODT tablets are supplied in unit dose blisters, 6 single units (2x3) per card, and 8 cards (48 tablets) per carton.

Each tablet contains 13.4 mg, 20.2 mg or 40.3 mg of prednisolone sodium phosphate (equivalent of 10 mg, 15 mg, or 30 mg of prednisolone respectively). The initial dose of Orapred ODT may vary from 10 to 60 mg (prednisolone base) per day, depending on the specific disease entity being treated. Use of an appropriate formulation of prednisolone was recommended if indicated dose cannot be obtained using Orapred ODT tablets, especially for treatments that require tapering the dose below 10 mg.

C. Basis for Approvability or Not-Approval Recommendation

The CMC information of the drug substance prednisolone sodium phosphate was referenced to the DMF [redacted]. This DMF has been recently reviewed and found to be adequate. Since the drug substance is a compendial item it is tested according to the USP specification and some additional tests such as residual solvents and additional impurities.

All ingredients in the drug product are of USP/NF grade except for the) [redacted]). [redacted] conforms to Ph. Eur.

Appropriate in-process, release and stability acceptance criteria have been established for the drug product to ensure consistency in quality. The packaging materials were found to be adequate. The drug product specification was considered adequate as revised.

The submitted drug product stability data for upto18 months conform to the established acceptance criteria. The submitted stability data was considered adequate to support the proposed 24-month expiration dating period.

The revised acceptance criterion of NMT [redacted] seconds for disintegration of the tablets is acceptable.

The proposed dissolution acceptance criterion of Q = [redacted] % in 30 minutes, as revised, is acceptable.

The NDA 21-959 is recommended for approval based on the submitted CMC information.

III. Administrative

A. Reviewer's Signature

Rao Puttagunta {electronic signature}

B. Endorsement Block

R.S. Harapanhalli {electronic signature}
Branch Chief, DPAMS, ONDQA

C. CC Block

N/A

APPEARS THIS WAY
ON ORIGINAL

48 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry- 1

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

/s/

Rao Puttagunta
5/25/2006 04:00:24 PM
CHEMIST

Ravi Harapanhalli
5/25/2006 04:12:52 PM
CHEMIST