

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020835

CHEMISTRY REVIEW(S)

DIVISION OF Metabolism and Endocrine DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 20-835 **CHEM. REVIEW #:** 2 **REVIEW DATE:** 2-23-98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	2-13-98	2-17-98	2-17-98
Correspondence	2-18-98	2-20-98	2-20-98

NAME & ADDRESS OF APPLICANT:

The Procter & Gamble Company
Sharon Woods Technical Center
11450 Grooms Road
Cincinnati, Ohio 4542-1434

DRUG PRODUCT NAME:

Proprietary: Actonel
Nonproprietary: Risedronate sodium
Chem. type/Ther. Class: 1 S (NME)

**APPEARS THIS WAY
ON ORIGINAL**

PHARMACOL. CATEGORY/INDICATION:

Treatment of Paget's disease of bone

DOSAGE FORM: Tablets (oral)

STRENGTHS: 30 mg tablets

ROUTE OF ADMINISTRATION: Oral

DISPENSED:

X **Rx** **OTC**

CHEMICAL NAMES, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:

Non-proprietary Name (USAN): Risedronate sodium

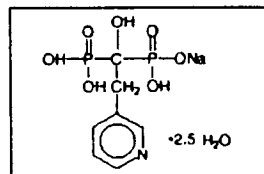
International Non-proprietary Name (INN): Risedronic acid

[The INN name is applied to the free acid form of risedronate sodium]

Chemical Name: [1-Hydroxy-2-(3-pyridinyl)ethylidene]- bis[phosphonic acid] monosodium salt hemi-pentahydrate

Chemical Name (CAS): 1-Hydroxy-1-phosphono-2-pyridin-3-yl-ethyl-phosphonic acid, monosodium salt

Chemical Name (IUPAC): 1-Hydroxy-1-phosphono-2-pyridin-3-yl-ethyl-phosphonic acid, monosodium salt



$C_7H_{10}NO_7P_2Na \cdot 2.5 H_2O$

Molecular Weight: Anhydrous: 305.10
Hemi-pentahydrate: 350.13

CAS #: 115436-72-1

SUPPORTING DOCUMENTS:**RELATED DOCUMENTS :**

CONSULTS: None

* Post approval, updates from the Actonel (30 mg tablets) stability program will be provided via Annual Report submissions.

* Any marketed product lots found to fall outside the approved specifications for the drug product will be reported to the FDA as required under CFR 314.81(b)(1)(ii)

* Procter & Gamble will identify any degradation products that are detected in their long term stability studies

CONCLUSIONS & RECOMMENDATIONS:

Satisfactory CMC information has been provided, and the application is approvable from a Chemistry point of view.

cc:
Orig. NDA 20-835
HFD-510/Division File
HFD-510/Sheldon Markofsky/2-23-98
HFD-510/R. Hedin (CSO)
HFD-510/M.Haber
HFD-510/D-G. Wu (Team Leader)
HFD-580/J. Gibbs

APPEARS THIS WAY
ON ORIGINAL

/S/

Sheldon Markofsky, Review Chemist

2-23-98

R/D Init by: Team Leader

filename: n20835.2

2/24/98

APPEARS THIS WAY
ON ORIGINAL

/S/

DIVISION OF Metabolism and Endocrine DRUG PRODUCTS
 Review of Chemistry, Manufacturing, and Controls

NDA#: 20-835 **CHEM. REVIEW #:** 1 **REVIEW DATE:** 1-29-98
 (Drug Product)

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
NDA (Original)	3-31-97	4-1-97	4-7-97
Amendment	7-25-97	7-28-97	7-30-97
Amendment	9-26-97	9-29-97	9-30-97
Amendment	10-16-97	10-17-97	10-20-97

NAME & ADDRESS OF APPLICANT:

The Procter & Gamble Company
 Sharon Woods Technical Center
 11450 Grooms Road
 Cincinnati, Ohio 4542-1434

DRUG PRODUCT NAME:

Proprietary: Actonel
Nonproprietary: Risedronate sodium
Chem. type/Ther. Class: 1 S (NME)

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 ON ORIGINAL

PHARMACOL. CATEGORY/INDICATION:

Treatment of Paget's disease of bone

DOSAGE FORM: Tablets (oral)

STRENGTHS: 30 mg tablets

ROUTE OF ADMINISTRATION: Oral

APPEARS THIS WAY
 ON ORIGINAL

DISPENSED: X Rx OTC

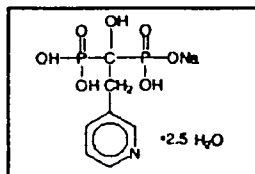
CHEMICAL NAMES, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.:

Non-proprietary Name (USAN): Risedronate sodium
 International Non-proprietary Name (INN): Risedronic acid
 [The INN name is applied to the free acid form of risedronate sodium]

Chemical Name: [1-Hydroxy-2-(3-pyridinyl)ethylidene]- bis[phosphonic acid] monosodium salt hemi-pentahydrate

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Molecular Weight: Anhydrous: 305.10
 Hemi-pentahydrate: 350.13

CAS #: 115436-72-1

SUPPORTING DOCUMENTS:**RELATED DOCUMENTS :****CONSULTS:** None**REMARKS/COMMENTS:**

Only the drug product portion of the NDA is fully reviewed here by this reviewer. Dr. Martin Haber has reviewed the drug substance.

The amendment dated 7-25-97 provides updated stability data for both the drug substance and the drug product. The 9-26-97 amendment provides for a categorical exclusion from the requirement of an Environmental Assessment, makes minor labeling changes, and corrects a minor error in an analytical method. Updated labeling was also provided in the amendment, dated 10-16-97

CONCLUSIONS & RECOMMENDATIONS:

From a chemistry point of view, this submission is approvable pending satisfactory response to the chemistry deficiencies.

cc:

Orig. NDA 20-835
 HFD-510/Division File
 HFD-510/Sheldon Markofsky/1-29
 HFD-510/R. Hedin (CSO)
 HFD-510/M.Haber
 HFD-510/D-G. Wu (Team Leader)
 HFD-580/J. Gibbs

APPEARS THIS WAY
 ON ORIGINAL

/S/

Sheldon Markofsky, Review Chemist

1-29-98

R/D Init by: Team Leader

filename: n20835a.wpd

1/30/98

/S/

APPEARS THIS WAY
 ON ORIGINAL