CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

017386Orig1s039

Trade Name:	ZAROXOLYN
Generic or Proper Name:	metolazone tablets
Sponsor:	UCB Inc.
Approval Date:	11/22/2013
Indication:	Indicated for the treatment of salt and water retention including: • Edema accompanying congestive heart failure; • Edema accompanying renal diseases including the nephrotic syndrome and states of diminished renal function. ZAROXOLYN is also indicated for the treatment of hypertension, alone or in combination with other antihypertensive drugs of a different class.

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 17386/S-039

APPROVAL LETTER

UCB Inc.
Attention: Ruta Monoenko
Senior Manager, Regulatory Affairs
1950 Lake Park Drive
Smyrna, GA 30080

Dear Ms. Monoenko:

Please refer to your Supplemental New Drug Application (sNDA) dated May 24, 2013, received May 28, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zaroxolyn® (metolazone) Tablets.

This "Changes Being Effected in 30 days" supplemental new drug application proposes to move the tests for tablet weight, thickness, and hardness from (b) (4)

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Yvonne Knight, Regulatory Project Manager, at (301) 796-2133.

Sincerely,

{See appended electronic signature page}

Hasmukh B. Patel, Ph.D.
Branch Chief
Branch III, Division of New Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

HASMUKH B PATEL
11/22/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

017386Orig1s039

CHEMISTRY REVIEW(S)

Office of New Drug Quality Assessment
Division of New Drug Quality Assessment I (Branch III)
Review of Chemistry, Manufacturing, and Controls

1. **NDA Supplement Number: NDA 17386 / S-039**

2. **Submission Being Reviewed**

Submission /Type	DARRTS SD Number	Submission Date	CDER Stamp Date	Assigned Date	PDUFA Goal Date	Review Date
S- 039 (CBE-30)	203	24-May-2013	28-May-2013	09-Jul-2013	28-Nov-2013	20-Nov-2013

3. **Proposed Changes:** This CBE-30 supplement proposes to move the tests for tablet weight, thickness, and hardness from [redacted] (b) (4)

4. **Review #:** 1

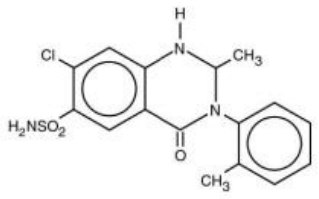
5. **Clinical Review Division:** Division of Cardiovascular and Renal Products

6. **Name and Address of Applicant:**
   UCB, Inc.
   Attention: Ruta Monoenko
   Senior Manager, Regulatory Affairs
   1950 Lake Park Drive
   Smyrna, GA 30080

7. **Drug Product:**

Drug Name	Dosage Form	Strength	Route of Administration	Rx or OTC
Zaroxolyn® Tablets (metolazone tablets, USP)	tablet	2½ mg, 5 mg, or 10 mg	oral	Rx

8. **Chemical name and structure of drug substance:**

	USAN: metolazone Chemical name: 7-chloro-1, 2, 3, 4-tetrahydro-2-methyl-3-(2-methylphenyl)-4-oxo-6-quinazolinesulfonamide Molecular formula: $C_{16}H_{16}ClN_3S$ MW: 365.83

9. **Pharmacological Category/Indication:** Metolazone is a diuretic indicated for the treatment of edema accompanying congestive heart failure or renal diseases and for the treatment of hypertension.

10. Supporting/Relating Document: N/A

11. Consults: N/A

12. Summary/Remarks

The purpose of this CBE-30 supplement is to move the three [redacted] (b) (4) (Tablet Weight, Thickness, and Hardness) to [redacted] (b) (4) This change is being proposed for the branded product, Zaroxolyn® Tablets, as well as the Authorized Generic, metolazone tablets, USP.

The applicant states that the purpose of these tests is to monitor tablet weight, thickness, and hardness [redacted] (b) (4) The applicant is not proposing to delete these tests; they will continue to be performed [redacted] (b) (4)

[redacted] (b) (4)

13. Conclusions & Recommendations:

This supplement is recommended for approval.

14. Comments/Deficiencies to be Conveyed to Applicant: None

15. Primary Reviewer: Sue-Ching Lin, CMC reviewer, ONDQA

Secondary Reviewer: Hasmukh Patel, Ph.D., Branch Chief, Branch III, Division of New Drug Quality Assessment I (DNDQA I), ONDQA

(See appended electronic signature page)

CMC Assessment

I. Background Information

NDA 17386 was approved in 1973. Metolazone is a quinazoline diuretic, with properties generally similar to the thiazide diuretics. Zaroxolyn® Tablets (metolazone tablets, USP) is indicated for the treatment of salt and water retention including:

- edema accompanying congestive heart failure;
- edema accompanying renal diseases, including the nephrotic syndrome and states of diminished renal function.

II. Proposed Changes

The purpose of this CBE-30 supplement is to move the three (b) (4) (Tablet Weight, Thickness, and Hardness) to (b) (4)

This change is being proposed for the branded product, Zaroxolyn® Tablets, as well as the Authorized Generic, metolazone tablets, USP.

Release Tests Being Moved to (b) (4)

Test	Acceptance Criteria[a]
Average Tablet Weight Deviation from Average Tablet Weight	(b) (4)
Thickness	
Hardness	

(b) (4)

III. Data Submitted to Support the Proposed Changes

The applicant states that the purpose of these tests (b) (4) tablet weight, thickness, and hardness (b) (4) The applicant is not proposing to delete these tests; (b) (4)

Evaluation: Acceptable. (b) (4) (b) (4) (b) (4)

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/s/

SUE CHING LIN
11/20/2013

NALLAPERUM CHIDAMBARAM
11/21/2013
for Dr. Hasmukh Patel

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APPLICATION NUMBER:

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ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 17386/S-039

CBE SUPPLEMENT – ACKNOWLEDGEMENT

UCB Inc.
Attention: Ruta Monoenko
Senior Manager, Regulatory Affairs
1950 Lake Park Drive
Smyrna, GA 30080

Dear Ruta Monoenko:

We have received your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA NUMBER: 17386

SUPPLEMENT NUMBER: 039

PRODUCT NAME: Zaroxolyn®, (metolazone) Tablets

DATE OF SUBMISSION: May 24, 2013

DATE OF RECEIPT: May 28, 2013

This supplemental application, submitted as a "Changes Being Effected in 30 days" supplement, proposes moving the test for tablet weight, thickness, and hardness from (b) (4)

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on July 27, 2013 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be November 28, 2013.

SUBMISSION REQUIREMENTS

Cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have questions please feel free to call me at (301) 796-2133.

Sincerely,

{See appended electronic signature page}

Yvonne Knight, MS
Regulatory Health Project Manager
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

YVONNE L KNIGHT
07/08/2013