



# RANBAXY

LABORATORIES LIMITED

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April 19, 1999

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

FEDERAL EXPRESS

Reference: Cefuroxime Axetil Tablets  
125 mg, 250 mg and 500 mg  
Abbreviated New Drug Application

Dear Sir/Madam:

Ranbaxy Laboratories Ltd. herewith submits an abbreviated new drug application (ANDA) for Cefuroxime Axetil Tablets, pursuant to Section 505 (j) of the Federal Food, Drug, and Cosmetic Act.

This ANDA refers to the listed drug Cefin<sup>®</sup> (Cefuroxime Axetil) tablets of Glaxo Wellcome Inc. Glaxo Wellcome Inc. is the holder of the approved application and is listed in the 1998 Approved Drug Products with Therapeutic Equivalence Evaluations, 18th Edition, page 3-68.

The manufacturer of the Cefuroxime Axetil drug substances used to produce the ANDA batches of the drug product is Ranbaxy Laboratories Limited, Mohali, Punjab, India. A sample of the bulk raw material is available and will be provided to the Agency upon request.

The drug product manufacturer is Ranbaxy Laboratories Limited, Dewas, India. Cefuroxime Axetil Tablets will be manufactured and packaged at Ranbaxy Laboratories Limited's manufacturing facility in accordance with 21 CFR 210 and 211. Ranbaxy Laboratories Limited in Dewas, India will also be responsible for the bulk drug substance release. The release and stability studies on the finished drug product are also carried out at the same location.

REGISTERED OFFICE SAHIBZADA AJIT SINGH NAGAR-160 055 DISTT. ROPAR (PUNJAB)

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**COMPARISON BETWEEN RANBAXY LABORATORIES LIMITED  
CEFUROXIME AXETIL TABLETS AND GLAXO-WELLCOME INC.  
CEFTIN<sup>®</sup> TABLETS  
[21 CFR 314.94(a)(4)-(6)]**

**1. Condition of Use:**

[21 CFR 314.94(a)(4)]

- a. The conditions of use prescribed, recommended or suggested in the labeling proposed for Cefuroxime Axetil Tablets have been previously approved for CEFTIN<sup>®</sup> Tablets.
- b. Refer to Ranbaxy Laboratories Ltd. annotated labeling and to the currently approved labeling for Ceftin<sup>®</sup> Tablets provided in Section V of this application.

**2. Active Ingredient(s):**

[21 CFR 314.94(a)(5)]

- a. The active ingredient of Ranbaxy Laboratories Ltd. Cefuroxime Axetil Tablets is a mixture of cefuroxime axetil (amorphous) and cefuroxime axetil (crystalline), whereas, the active ingredient of Ceftin<sup>®</sup> Tablets is amorphous cefuroxime axetil.
- b. Refer to Ranbaxy Laboratories Ltd. annotated labeling and to the currently approved labeling for Ceftin<sup>®</sup> Tablets provided in Section V of this application.

**3. Route of Administration, Dosage Form and Strength:**

[21 CFR 314.94(a)(6)]

- a. The route of administration, dosage form, and strength for Ranbaxy Laboratories Ltd. Cefuroxime Axetil Tablets are the same as Ceftin<sup>®</sup> Tablets.
- b. Refer to Ranbaxy Laboratories Ltd. annotated labeling and to the current approved labeling for Ceftin<sup>®</sup> Tablets provided in Section V of this application.

4. Side-by-Side Comparison of information demonstrating that the proposed product is the same as the listed product:

	Proposed Drug: Cefuroxime Axetil Tablets	Listed Drug: Ceftin Tablets
Condition of use:	<p><b>INDICATIONS AND USAGE</b> Cefuroxime Axetil tablets are indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below:</p> <ol style="list-style-type: none"> <li>1. <b>Pharyngitis/Tonsillitis</b> caused by <i>Streptococcus pyogenes</i>. NOTE: The usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever, is penicillin given by the intramuscular route. Cefuroxime axetil tablets are generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefuroxime in the subsequent prevention of rheumatic fever are not available. Please also note that in all clinical trials, all isolates had to be sensitive to both penicillin and cefuroxime. There are no data from adequate and well-controlled trials to demonstrate the effectiveness of cefuroxime in the treatment of penicillin-resistant strains of <i>Streptococcus pyogenes</i>.</li> <li>2. <b>Acute Bacterial Otitis Media</b> caused by <i>Streptococcus pneumoniae</i>, <i>Haemophilus influenzae</i> (including beta-lactamase-producing strains), <i>Moraxella catarrhalis</i> (including beta-lactamase-producing strains), or <i>Streptococcus pyogenes</i>.</li> <li>3. <b>Acute Bacterial Maxillary Sinusitis</b> caused by <i>Streptococcus pneumoniae</i> or <i>Haemophilus influenzae</i> (non-beta-lactamase-producing strains only). (See CLINICAL STUDIES section.) NOTE: In view of the insufficient numbers of isolates of beta-</li> </ol>	<p><b>INDICATIONS AND USAGE</b> CEFTIN Tablets are indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below:</p> <ol style="list-style-type: none"> <li>1. <b>Pharyngitis/Tonsillitis</b> caused by <i>Streptococcus pyogenes</i>. NOTE: The usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever, is penicillin given by the intramuscular route. CEFTIN Tablets are generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefuroxime in the subsequent prevention of rheumatic fever are not available. Please also note that in all clinical trials, all isolates had to be sensitive to both penicillin and cefuroxime. There are no data from adequate and well-controlled trials to demonstrate the effectiveness of cefuroxime in the treatment of penicillin-resistant strains of <i>Streptococcus pyogenes</i>.</li> <li>2. <b>Acute Bacterial Otitis Media</b> caused by <i>Streptococcus pneumoniae</i>, <i>Haemophilus influenzae</i> (including beta-lactamase-producing strains), <i>Moraxella catarrhalis</i> (including beta-lactamase-producing strains), or <i>Streptococcus pyogenes</i>.</li> <li>3. <b>Acute Bacterial Maxillary Sinusitis</b> caused by <i>Streptococcus pneumoniae</i> or <i>Haemophilus influenzae</i> (non-beta-lactamase-producing strains only). (See CLINICAL STUDIES section.) NOTE: In view of the insufficient numbers of isolates of beta-</li> </ol>

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	Proposed Drug: Cefuroxime Axetil Tablets	Listed Drug: Ceftin <sup>®</sup> Tablets
	<p>lactamase-producing strains of <i>Haemophilus influenzae</i> and <i>Moraxella catarrhalis</i> that were obtained in clinical trials with cefuroxime axetil tablets for patients with acute bacterial maxillary sinusitis, it was not possible to adequately evaluate the effectiveness of cefuroxime axetil tablets for sinus infections known, suspected, or considered potentially to be caused by beta-lactamase-producing <i>Haemophilus influenzae</i> or <i>Moraxella catarrhalis</i>.</p> <p>4. Acute Bacterial Exacerbations of Chronic Bronchitis and Secondary Bacterial Infections of Acute Bronchitis caused by <i>Streptococcus pneumoniae</i>, <i>Haemophilus influenzae</i> (beta-lactamase negative strains), or <i>Haemophilus parainfluenzae</i> (beta-lactamase negative strains). (See DOSAGE AND ADMINISTRATION section and CLINICAL STUDIES section.)</p> <p>5. Uncomplicated Skin and Skin-Structure Infections caused by <i>Staphylococcus aureus</i> (including beta-lactamase-producing strains) or <i>Streptococcus pyogenes</i>.</p> <p>6. Uncomplicated Urinary Tract Infections caused by <i>Escherichia coli</i> or <i>Klebsiella pneumoniae</i>.</p> <p>7. Uncomplicated Gonorrhea, urethral and endocervical, caused by penicillinase-producing and non-penicillinase-producing strains of <i>Neisseria gonorrhoeae</i> and uncomplicated gonorrhea, rectal, in females, caused by non-penicillinase-producing strains of <i>Neisseria gonorrhoeae</i>.</p> <p>8. Early Lyme Disease (erythema migrans) caused by <i>Borrelia burgdorferi</i>.</p> <p>Culture and susceptibility testing should be performed when appropriate to determine susceptibility of the causative microorganism(s) to cefuroxime. Therapy</p>	<p>lactamase-producing strains of <i>Haemophilus influenzae</i> and <i>Moraxella catarrhalis</i> that were obtained in clinical trials with CEFTIN Tablets for patients with acute bacterial maxillary sinusitis, it was not possible to adequately evaluate the effectiveness of CEFTIN Tablets for sinus infections known, suspected, or considered potentially to be caused by beta-lactamase-producing <i>Haemophilus influenzae</i> or <i>Moraxella catarrhalis</i>.</p> <p>4. Acute Bacterial Exacerbations of Chronic Bronchitis and Secondary Bacterial Infections of Acute Bronchitis caused by <i>Streptococcus pneumoniae</i>, <i>Haemophilus influenzae</i> (beta-lactamase negative strains), or <i>Haemophilus parainfluenzae</i> (beta-lactamase negative strains). (See DOSAGE AND ADMINISTRATION section and CLINICAL STUDIES section.)</p> <p>5. Uncomplicated Skin and Skin-Structure Infections caused by <i>Staphylococcus aureus</i> (including beta-lactamase-producing strains) or <i>Streptococcus pyogenes</i>.</p> <p>6. Uncomplicated Urinary Tract Infections caused by <i>Escherichia coli</i> or <i>Klebsiella pneumoniae</i>.</p> <p>7. Uncomplicated Gonorrhea, urethral and endocervical, caused by penicillinase-producing and non-penicillinase-producing strains of <i>Neisseria gonorrhoeae</i> and uncomplicated gonorrhea, rectal, in females, caused by non-penicillinase-producing strains of <i>Neisseria gonorrhoeae</i>.</p> <p>8. Early Lyme Disease (erythema migrans) caused by <i>Borrelia burgdorferi</i>.</p> <p>Culture and susceptibility testing should be performed when appropriate to determine susceptibility of the causative microorganism(s) to cefuroxime. Therapy</p>

	<b>Proposed Drug:</b> Cefuroxime Axetil Tablets	<b>Listed Drug:</b> Ceftin <sup>®</sup> Tablets
	may be started while awaiting the results of this testing. Antimicrobial therapy should be appropriately adjusted according to the results of such testing.	may be started while awaiting the results of this testing. Antimicrobial therapy should be appropriately adjusted according to the results of such testing.
<b>Active Ingredient(s)</b>	Cefuroxime axetil	Cefuroxime axetil
<b>Dosage Form</b>	Tablets	Tablets
<b>Route of Administration:</b>	Oral	Oral
<b>Strengths:</b>	125 mg , 250 mg and 500 mg	125 mg , 250 mg and 500 mg

Ceftin<sup>®</sup> = Cefuroxime axetil, Glaxo Wellcome Inc.

**Bioequivalency Data:** Refer to Section VI of this application for information required as evidence of *in-vivo* bioequivalence between the listed product and the proposed product.

**Labeling:** Refer to Section V for copies of the current labeling for the listed drug, Ceftin<sup>®</sup> Tablets and labeling for the product proposed in this application.

**Annotated Side- by- Side Labeling Comparison (Contd.)**

c. **Similarities and Differences Between Inserts (by insert section)**

**I. PRODUCT NAME**

**A. Differences**

1. The innovator trade name is not used by Ranbaxy Laboratories Limited.
2. The proposed labeling does not include powder for oral suspension.
3. The innovator's statement on dispensing "Rx" has been replaced by "Rx only" in the proposed labeling.

**II. DESCRIPTION**

**A. Differences**

1. The innovator trade name is not used by Ranbaxy Laboratories Limited.
2. All references to CEFTIN<sup>®</sup> has been omitted from the proposed labeling.
3. The following inactive ingredients in the proposed labeling are not found in innovator labeling: [ ]
4. The following inactive ingredients in the innovator labeling under Ceftin Tablets are not found in proposed labeling: hydrogenated vegetable oil, hydroxypropyl methylcellulose, methyl paraben, propylene glycol, propyl paraben, sodium benzoate and titanium dioxide.
5. All references to powder for oral suspension, found in Innovator labeling are omitted in the proposed labeling.

All other text is identical.

R 0377e

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CONFIDENTIAL MATERIAL OMITTED -- MATERIAL SUBJECT TO PROTECTIVE ORDER ENTERED DECEMBER 11, 2000 IN CASE NO. 00-5172 (MLC) BEFORE THE U.S. DISTRICT COURT FOR THE DISTRICT OF NEW JERSEY

DESCRIPTION OF MATERIAL OMITTED: TECHNICAL INFORMATION FROM RANBAXY'S ANDA