DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 019537/S-086
NDA 019847/S-057
NDA 019857/S-065
NDA 020780/S-043
NDA 021473/S-037

SUPPLEMENT APPROVAL

Bayer HealthCare Pharmaceuticals, Inc.
Attention: Joseph Marini, MS, RPh
Associate Director, Regulatory Affairs – Established Products
100 Bayer Blvd.
PO Box 0915
Whippany, NJ 07981-0915

Dear Mr. Marini:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received June 10, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA #	Supplement #	Drug Product	Dosage
019537	S-086	CIPRO (ciprofloxacin hydrochloride) Tablets	250 mg, 500 mg, and 750 mg
019847	S-057	CIPRO (ciprofloxacin hydrochloride) 1% Solution in vials	200 mg/20 mL and 400 mg/40 mL
019857	S-065	CIPRO (ciprofloxacin hydrochloride) 0.2% Solution in 5% Dextrose	200 mg and 400 mg
020780	S-043	CIPRO (ciprofloxacin hydrochloride) Oral Suspension	5% and 10%
021473	S-037	CIPRO XR (ciprofloxacin extended-release) Tablets	500 mg and 1000 mg

We also refer to our letter dated May 12, 2016, notifying you, under Section 505(o)(4) of the FDCA, of new safety information required to be included in the labeling for the systemic fluoroquinolone class of antibacterial drugs.

These sNDAs provide for revisions to the Indications and Usage section of the package insert to include a new limitation of use statement for acute exacerbation of chronic bronchitis, uncomplicated urinary tract infections, acute uncomplicated cystitis, and acute sinusitis to reserve CIPRO, and CIPRO XR, for treatment in patients who have no alternative treatment options. In addition, the Boxed Warning, Warnings and Precautions, and Information for Patients sections of the package insert and the Medication Guide have been revised to include information regarding the risk of disabling and potentially irreversible serious adverse reactions.

Other label changes not required under section 505(o)(4) were also provided so as to furnish adequate information for the safe and effective use of CIPRO and CIPRO XR.

These amended supplemental new drug applications provide for all revisions to the labeling for CIPRO and CIPRO XR consistent with our May 12, 2016 letter.

APPROVAL & LABELING

We have completed our review of these supplemental applications. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in these supplemental applications, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Susmita Samanta, Safety Regulatory Project Manager, at (301) 796-0803.

Sincerely,

{See appended electronic signature page}

Joseph G. Toerner, M.D., M.P.H.
Deputy Director for Safety
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

JOSEPH G TOERNER
07/26/2016