



NDA 50-006/S-089
NDA 50-007/S-032
NDA 50-442/S-020
NDA 50-480/S-056
NDA 50-533/S-045

SUPPLEMENT APPROVAL

Pfizer, Inc
Attention: Michele Burtness
Senior Manager, Pfizer Essential Health Global Regulatory Affairs Brands
235 East 42nd Street
New York, NY 10017

Dear Ms. Burtness:

Please refer to your Supplemental New Drug Applications (sNDAs) dated November 21, 2016, received November 21, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA Number	Drug Product	Supplement Number
NDA 50-006	Vibramycin (doxycycline monohydrate) for Oral Suspension	S-089
NDA 50-007	Vibramycin (doxycycline hyclate capsules, USP) Capsules	S-032
NDA 50-442	Vibramycin (doxycycline hyclate)	S-020
NDA 50-480	Vibramycin (doxycycline calcium for Oral Suspension	S-056
NDA 50-533	Vibra-tabs (doxycycline hyclate, USP) Film Coated Tabs	S-045

These Prior Approval supplemental new drug applications provide for changes to the **WARNINGS** and **ADVERSE REACTIONS** sections of the labeling as outlined below:

WARNINGS

Severe skin reactions, such as exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in patients receiving doxycycline. (See ADVERSE REACTIONS.) If severe skin reactions occur, doxycycline should be discontinued immediately and appropriate therapy should be instituted.

ADVERSE REACTIONS

Gastrointestinal: anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region, and pancreatitis. Hepatotoxicity has been reported rarely. These reactions have been caused by both the oral and parenteral administration of tetracyclines. Superficial discoloration of the adult permanent dentition, reversible upon drug discontinuation and professional dental cleaning has been reported. Permanent tooth discoloration and enamel hypoplasia may occur with drugs of the tetracycline class when used during tooth development. (See WARNINGS.)

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is 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 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.

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Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, 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 this supplemental application, 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 Carmen DeBellas, Regulatory Project Manager, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

Dmitri Iarikov, MD, PhD
Acting Deputy Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
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/

DMITRI IARIKOV
07/26/2017