



NDA 20-239/S-016 & S-017

Hoffman-La Roche Inc.
Attention: Christine Hoogmoed
Senior C.M.C. Associate
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Ms. Hoogmoed:

Please refer to your supplemental new drug applications dated May 17, 2004, received May 18, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Kytril[®] Injection.

These supplemental applications provide for the following:

1. S-016 provides for a change in formulation to add a 0.1 mg/1 mL single-use vial and
2. S-017 provides for the addition of an alternate secondary packaging site in Kaiseraugst, Switzerland for the 1 mg/1 mL vial and 4 mg/4 mL vial.

We completed our review of these applications. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the following requested minor editorial revisions listed below in double-underline:

1. The submitted draft vial label (27898742-L 5/13/04) is missing the stated volume "1" for the vial and should read as follows:

"0.1 mg/1mL
Single-Use Vial"

and be located above the drug name "Kytril[®]".

2. The submitted draft carton label for 1 vial (27898741-C 5/13/04) is missing the stated volume "1" for the vial size in two locations contained in the carton and should read as follows:

"0.1 mg/1 mL"

and be located in the middle of the front panel below the established name as well as

"1 x 0.1 mg/1mL"
Single-Use Vial"

and be located at the bottom of the front panel below the Rxonly text respectively.

3. The submitted draft carton label for 5 vials (2789XXX) is missing the stated volume “1” for the vial size in 4 locations (includes the photograph of the Kytril[®] vial) contained in the carton and should read as follows:

“0.1 mg/1 mL”

and be located in the middle of the front panel below the established name and as

“5 x 0.1 mg/1mL Single-Use Vials”

and be located at the bottom of the front panel below the Rxonly text, as well as the changes in #1 above to address the changes needed to include the 1 mL vial photograph located on the right side of the front panel.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the package insert (May2004) submitted May 17, 2004, container label (27898742-L) submitted May 17, 2004, carton for 1 vial (277898741-C) submitted May 17, 2004 and carton for 5 vials (2789XXXX) submitted May 17, 2004.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling is to be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper.

This submission should be designated "FPL for approved supplement NDA 20-239/S-016." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Betsy Scroggs, Pharm.D., Consumer Safety Officer at (301) 827-1250.

Sincerely,

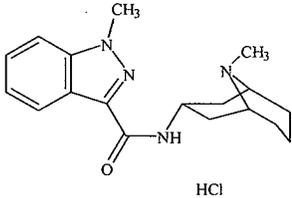
{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Acting Director
Division of Gastrointestinal and Coagulation Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Joyce Korvick
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CHEMIST'S REVIEW 3		1. Organization: HFD-180	2. NDA Number: 20-239
3. Name and Address of Applicant (City & State): Hoffmann-La Roche Inc. 340 Kingland Street Nutley, NJ 07110-1199		4. AF Number:	
6. Name of Drug: Kytril		7. Nonproprietary Name: Granisetron Hydrochloride	Supplement (s) Number (s) Date (s) SCF-016 May 17, 2003 SCM-017
8. Supplement Provides for <ul style="list-style-type: none"> New, low-dosage strength 0.1 mg/1ml of Kytril injection Alternative secondary packaging site for the other two dosing strengths 		9. Amendments and Other (Reports, etc.) Dates: SCF-015-AC April 20, 2004	
10. Pharmacological Category: Anti-emetic	11. How Dispensed: Rx	12. Related IND/NDA/DMF (s): None	
13. Dosage Form: Injection-Intravenous	14. Potency: 0.1 mg/mL		
15. Chemical Name and Structure: <div style="text-align: center;">  <p>HCl</p> </div> <p>endo -N-(9-methyl-9-azabicyclo [3.3.1] non-3-yl)-1-methyl-1H-indazole-3-carboxamide hydrochloride</p>		16. Records and Reports:	
		Current Yes No	
		Reviewed Yes x No	
17. Comments: See Review Notes. HFD-180/Div File HFD-181/CSO/BStrongin HFD-180/JKorvick HFD-180/ZGe HFD-180/AAlhakim R/D init by:LZhou			
18. Conclusions and Recommendations: This supplement may be approved based on CMC point of view, pending Clinical and Biopharm concurrence.			
19. Reviewer			
Name: Zhengfang Ge	Signature	Date Completed: Aug 25, 2004	

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✓ § 552(b)(4) Trade Secret /
Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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/s/

Zhengfang Ge
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CHEMIST

Ali Al-Hakim
8/30/04 02:43:24 PM
CHEMIST
Ali Al-Hakim for Liang Zhou



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-039/S-016 & S-017

Hoffman-La Roche Inc.
Attention: Christine Hoogmoed
Senior C.M.C. Associate
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Ms. Hoogmoed:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Kytril® Injection
NDA Number: 20-049
Supplement numbers: 016 & 017
Date of supplements: May 17, 2004
Date of receipt: May 18, 2004

As noted above, the submission has been administratively split into two supplements to clearly delineate and track the two requested changes.

These supplemental applications provide for the following:

1. S-016 provides for a change in formulation to add a ~~1~~ mL single-use vial and
2. S-017 provides for the addition of an alternate secondary packaging site in Kaiseraugst, Switzerland for the 1 mg/1 mL vial and 4 mg/4 mL vial.

b(4)

Unless we notify you within 60 days of the receipt date that these applications are not sufficiently complete to permit a substantive review, we will file these applications on July 17, 2004 in accordance with 21 CFR 314.101(a). If these applications are filed, the user fee goal date will be September 18, 2004.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service or Courier/Overnight Mail:

Center for Drug Evaluation and Research
Division of Gastrointestinal and Coagulation Drug Products
Attention: Document Room 8B-45
5600 Fishers Lane
Rockville, Maryland 20857

Request: Please provide electronic copies of your proposed package insert, currently approved package insert, and marked up version in PDF and Word in order to facilitate the review of S-016.

Please contact me if you have any questions by calling me at (301) 827-1250.

Sincerely,

{See appended electronic signature page}

Betsy Scroggs, Pharm. D.
Consumer Safety Officer
Division of Gastrointestinal and Coagulation Drug Products, HFD 180
Center for Drug Evaluation and Research

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/s/

Betsy Scroggs
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