DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 075218

LABELING ORDER

Baxter Healthcare Corporation
J. Barton Kalis
Regulatory Affairs
2 Esterbrook Lane
Cherry Hill, NJ 08003

Dear Mr. Kalis:

Please refer to your abbreviated new drug application (ANDA) submitted under section 505(j) of the Federal Food, Drug and Cosmetic Act (FDCA) for Vecuronium Bromide for Injection, 10 mg/mL and 20 mg/mL.

On September 17, 2010, we sent you a letter invoking our authority under section 505(o)(4) of the FDCA to require safety related label changes to the labeling of Vecuronium Bromide for Injection, USP to address the risk of anaphylactic and anaphylactoid type adverse reactions with the use of neuromuscular blockers. The decision to require safety labeling changes was based on new safety information about this risk identified since this product was approved on August 23, 1999. You were directed to submit, within 30 days of the date of that letter, a prior approval supplement proposing changes to the approved labeling, or notify FDA that you do not believe a labeling change is warranted, and submit a statement detailing the reasons why such a change is not warranted.

The 30 days have passed and we have not received any submission from you addressing our letter dated September 17, 2010.

You failed to respond to our September 17, 2010, letter within 30 days. Under the authority of section 505(o)(4)(E) of the FDCA, we are ordering you to make all of the changes in the labeling listed in the September 17, 2010, letter (attached).

Pursuant to section 505(o)(4)(E) of the FDCA, a supplement containing all of the changes to the labeling that are listed in the September 17, 2010 letter, must be received by FDA by November 16, 2010, for Vecuronium Bromide for Injection.

Alternatively, by November 6, 2010, you may appeal this Order using the Agency's established formal dispute resolution process as described in 21 CFR 10.75 and the Guidance for Industry, "Formal Dispute Resolution: Appeals Above the Division Level." The appeal should be submitted as correspondence to your ANDA referenced above. Identify the submission as "**Formal Dispute Resolution Request**" both on the cover letter and on the outside envelope. A copy of the submissions should be sent to:

Director
Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Mail Code HFD-600
7500 Standish Place
Rockville, MD 20855

In addition, to expedite coordination of any such appeal, a copy of the submission should also be sent to:

Carrie Lemley
Labeling Project Manager
Division of Labeling and Program Support
MPN 1
7520 Standish Place
Rockville, MD 20855

Refer to the Guidance for Industry, "Formal Dispute Resolution: Appeals Above the Division Level" for further instruction regarding the content and format of your request. Questions regarding the formal dispute resolution process may be directed to Kim Quaintance at (301) 796-0140. Appeals received by the Agency later than November 6, 2010, will not be entertained.

Failure to respond to this Order within the specified timeframes is a violation of section 505(o)(4) of the FDCA and could subject you to civil monetary penalties under section 303(f)(4) of the FDCA, 21 U.S.C. 333(f)(4), in the amount of up to $250,000 per violation, with additional penalties if the violation continues uncorrected. Further, such a violation would cause your product to be misbranded under section 502(z) of the Act, 21 U.S.C. 352(z), which could subject you to additional enforcement actions, including but not limited to seizure of your product and injunction.

If you have any questions, call Carrie Lemley, Labeling Project Manager, at (240) 276-8986.

Sincerely,

{See appended electronic signature page}

Helen Winkle
Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

ENCLOSURE: Safety Labeling Change Notification Letter

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 075218

SAFETY LABELING CHANGE NOTIFICATION

Baxter Healthcare Corporation
Regulatory Affairs
2 Esterbrook Lane
Cherry Hill, NJ 08003

To Whom It May Concern:

Please refer to your abbreviated new drug application (ANDA) for Vecuronium Bromide for Injection, 10 mg/mL and 20 mg/mL.

SAFETY LABELING CHANGES

Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to make safety related label changes based upon new safety information that becomes available after approval of the drug or biological product.

Section 505(o)(4) also authorizes FDA to require the holder of an approved application under section 505(j) (an ANDA) to make safety related label changes based upon new safety information if the same drug approved under section 505(b) is not currently marketed. You are the holder of an ANDA which references a drug approved under section 505(b) that is not currently marketed.

Since Vercuronium Bromide was approved on August 23, 1999, we have become aware of postmarketing cases of anaphylactic and anaphylactoid type adverse reactions, including fatalities, reported in association with use of neuromuscular blockers, including Vercuronium Bromide. Analyses of reports received through the Adverse Event Reporting System have shown occurrence of anaphylactic and anaphylactoid type adverse reactions with use of neuromuscular blockers, both depolarizing and non-depolarizing. We consider this information to be “new safety information” as defined in section 505-1(b)(3) of FDCA.

In accordance with section 505(o)(4) of the FDCA, we are notifying you that based on the new safety information described above, we believe that the new safety information should be included in the labeling for Vercuronium Bromide as follows:

Add the following to the **WARNINGS** section:

WARNINGS
Anaphylaxis
Severe anaphylactic reactions to neuromuscular blocking agents, including VERCURONIUM BROMIDE, have been reported. These reactions have in some cases been life-threatening and fatal. Due to the potential severity of these reactions, the necessary precautions, such as the immediate availability of appropriate emergency treatment, should be taken. Precautions should also be taken in those individuals who have had previous anaphylactic reactions to other neuromuscular blocking agents since cross-reactivity between neuromuscular blocking agents, both depolarizing and non-depolarizing, has been reported in this class of drugs.

Add the following to the **PRECAUTIONS** section:

PRECAUTIONS

Since allergic cross-reactivity has been reported in this class, request information from your patients about previous anaphylactic reactions to other neuromuscular blocking agents. In addition, inform your patients that severe anaphylactic reactions to neuromuscular blocking agents, including VERCURONIUM BROMIDE have been reported.

Add the following to the **ADVERSE REACTIONS** section:

ADVERSE REACTIONS

There have been post-marketing reports of severe allergic reactions (anaphylactic and anaphylactoid reactions) associated with use of neuromuscular blocking agents, including VERCURONIUM BROMIDE. These reactions, in some cases, have been life-threatening and fatal. Because these reactions were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency (See **WARNINGS** and **PRECAUTIONS**).

In accordance with section 505(o)(4), within 30 days of the date of this letter, you must submit a prior approval supplement proposing changes to the approved labeling in accordance with the above direction, or notify FDA that you do not believe a labeling change is warranted, and submit a statement detailing the reasons why such a change is not warranted. Requirements under section 505(o)(4) apply to NDAs, BLAs, and ANDAs without a currently marketed reference listed drug approved under an NDA, including discontinued products, unless approval of an application has been withdrawn in the Federal Register. Therefore, the requirements described in this letter apply to you, unless approval of your application has been withdrawn in the Federal Register.

Under section 502(z), failure to submit a response in 30 days may subject you to enforcement action, including civil money penalties under section 303(f)(4)(A) and an order

to make whatever labeling changes FDA deems appropriate to address the new safety information.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

SAFETY LABELING CHANGES UNDER 505(o)(4)
PRIOR APPROVAL SUPPLEMENT
OR

SAFETY LABELING CHANGES UNDER 505(o)(4)
CHANGE NOT WARRANTED

Prominently identify subsequent submissions related to the safety labeling changes supplement with the following wording in bold capital letters at the top of the first page of the submission:

SUPPLEMENT <<insert assigned #>>
SAFETY LABELING CHANGES UNDER 505(o)(4)-AMENDMENT

If you have any questions, call Ann (Thuyahn) Vu, Labeling Reviewer, at (240) 276-8991

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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

/s/

ROBERT L WEST

09/17/2010

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

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

/s/

EDWARD M SHERWOOD on behalf of HELEN N WINKLE
11/02/2010