CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

Approval Letter

ANDA 75-164

OCT 21 1999

Abbott Laboratories
Attention: Jill Sackett
200 Abbott Park Road, D-389 AP 30
Abbott Park, IL 60064-3537

Dear Madam:

This is in reference to your abbreviated new drug application dated June 30, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Vecuronium Bromide for Injection, 10 mg/vial and 20 mg/vial. The 10 mg/vial strength is packaged both with and without a 10 mL vial of diluent (Bacteriostatic Water for Injection, USP).

Reference is also made to your amendment dated September 13, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Vecuronium Bromide for Injection, 10 mg/vial and 20 mg/vial, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Norcuron Injection, 10 mg/vial and 20 mg/vial, respectively, of Organon, Inc.).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/ - 10/21/99

Douglas L. Spörn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

FINAL PRINTED LABELING

For reconstitution see other panel
WARNING. Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available
Usual Dosage/Storage: See package insert.
Lot
Caution: Federal (USA) law prohibits dispensing without prescription.
Exp
Lot

CHECK APPROPRIATE BOX
Reconstituted with supplied bacteriostatic water for injection (contains benzyl alcohol) not for use in newborns. Use within 5 days of
Date Prepared Time
OR
Reconstituted with sterile water for injection or compatible I.V. solutions (see package insert). Single use only. Discard unused portion within 24 hours of
Date Prepared Time
RAC5744-2/R3-1/98

NDC 0074-1632-01
VECURONIUM BROMIDE FOR INJECTION
10 mg* FOR IV USE ONLY
PROTECT FROM LIGHT
*1 mg/mL when reconstituted to 10 mL.
ABBOTT LABS., N. CHGO., IL 60064, USA

For reconstitution see other panel
WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.
Usual Dosage/Storage: See package insert
Exp
Lot 21

CHECK APPROPRIATE BOX

Reconstituted with supplied bacteriostatic water for injection: Contains benzyl alcohol, not for use in newborns. Use within 5 days of:

Date Prepared | OR | Time

Reconstituted with sterile water for injection or compatible I.V. solutions (per package insert). Single use only. Discard unused portion within 24 hours of:

Date Prepared | Time

Caution: Federal (USA) law prohibits dispensing without prescription.
RAO5724-2/R2-1/98

NDC 0074-1634-01
VECURONIUM BROMIDE FOR INJECTION
20 mg*
FOR IV USE ONLY
PROTECT FROM LIGHT
*1 mg/mL when reconstituted to 20 mL.
ABBOTT LABS., N. CHICAGO, IL 60064, USA

10 mL Flip-Top Vial

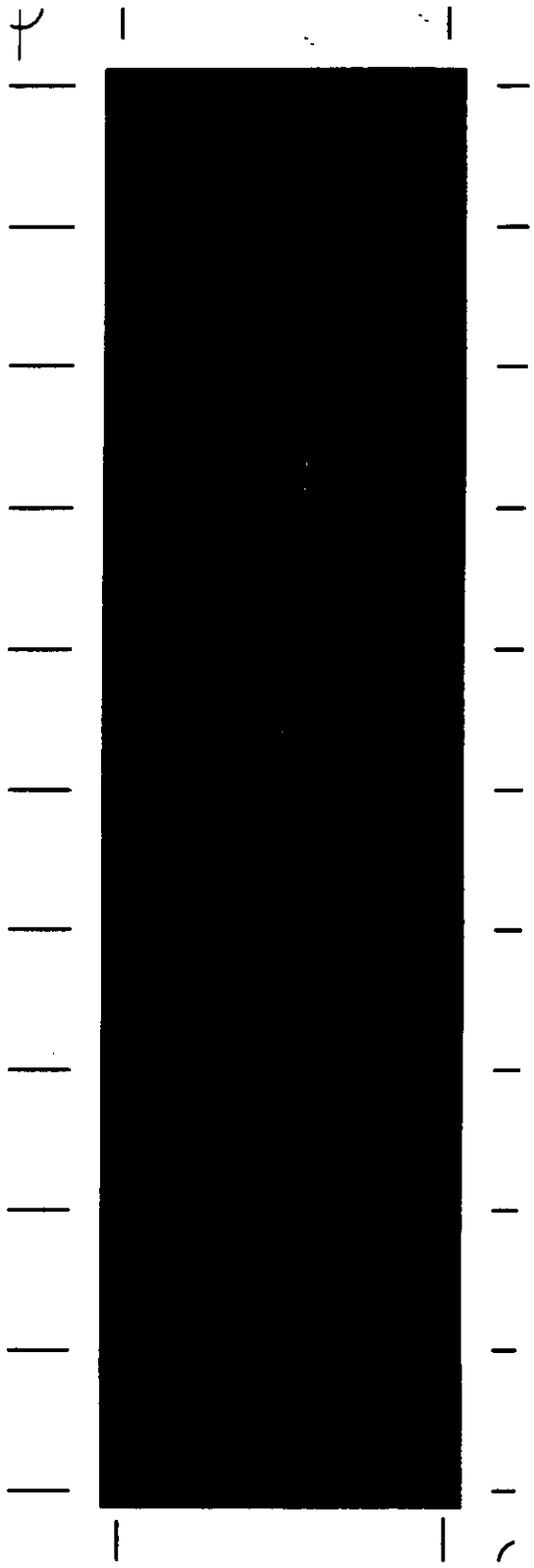
FOR DRUG DILUENT USE ONLY.
NOT FOR USE IN NEWBORNS.

ABBOTT LABS., NORTH CHICAGO, IL 60064, USA

NDC 0074-3977-10

0.9% benzyl alcohol added
Sterile, nonpyrogenic. Store at controlled room temperature 15° to 30°C (59° to 86°F). Caution: Federal (USA) law prohibits dispensing without prescription.

RAO 5723-4/R2-1/98



10 vials, lyophilized powder

10 Units/**NDC 0074-1632-01**

VECURONIUM BROMIDE FOR INJECTION

10 mg*

FOR IV SINGLE USE ONLY

***1 mg/mL** when reconstituted to **10 mL**.

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

Storage: Store dry powder at controlled room temperature 15° to 30°C (59° to 86°F).
PROTECT FROM LIGHT.
When reconstituted with bacteriostatic water for injection: **CONTAINS BENZYL ALCOHOL WHICH IS NOT FOR USE IN NEWBORNS.** Use within 5 days. May be stored at room temperature or refrigerated.
If reconstituted with sterile water for injection or other compatible I.V. solutions (per package insert): Refrigerate vial. Use within 24 hours. Single use only.
Discard unused portion.
Caution: Federal (USA) law prohibits dispensing without prescription.
WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

RAO574-2/R2-1/98

Printed in USA

Exp

Lot

(01) 1 030074 163201 8

10 vials

VECURONIUM BROMIDE FOR INJECTION

10 mg* FOR IV SINGLE USE ONLY

No Refrigeration Required

10 vials, lyophilized powder

10 Units/**NDC 0074-1632-01**

VECURONIUM BROMIDE FOR INJECTION

10 mg*

FOR IV SINGLE USE ONLY

***1 mg/mL** when reconstituted to **10 mL**.

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

When reconstituted with 10 mL of sterile water for injection the resultant solution will contain per mL:

vecuronium bromide	1 mg
citric acid anhydrous, USP	2.075 mg
sodium phosphate dibasic anhydrous, USP	1.625 mg
mannitol, USP (to adjust tonicity)	9.7 mg

May contain sodium hydroxide and/or phosphoric acid for pH adjustment. pH 4 (3.5 to 4.5).

Usual Dosage: Read enclosed prescribing information.

10 x 10 mL vials (powder)
10 x 10 mL vials (diluent)

VECURONIUM BROMIDE FOR INJECTION with diluent

10 mg*

FOR IV USE ONLY

No Refrigeration Required

Exp.

Lot

(01) 1 030074 161301 7

10 vials lyophilized powder. 10 vials of bacteriostatic water for injection, USP.

Store dry powder at controlled room temperature 15° to 30°C (59° to 86°F). **PROTECT FROM LIGHT.**
When reconstituted with supplied bacteriostatic water for injection: **CONTAINS BENZYL ALCOHOL WHICH IS NOT FOR USE IN NEWBORNS.** Use within 5 days. May be stored at room temperature or refrigerated.
If reconstituted with sterile water for injection or other compatible I.V. solutions (per package insert): Refrigerate vial. Use within 24 hours. Single use only. Discard unused portion.
Caution: Federal (USA) law prohibits dispensing without prescription.
WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

RAO5722-2/R2-1/98

Printed in USA

10 x 10 mL vials (powder)
10 x 10 mL vials (diluent)

10 Units/**NDC 0074-1613-01**

VECURONIUM BROMIDE FOR INJECTION with diluent

10 mg*

FOR IV USE ONLY

***1 mg/mL** when reconstituted with **10 mL** of bacteriostatic water for injection, USP.

10 vials lyophilized powder.

10 vials of bacteriostatic water for injection, USP.

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

10 x 10 mL vials (powder)
10 x 10 mL vials (diluent)

10 Units/**NDC 0074-1613-01**

VECURONIUM BROMIDE FOR INJECTION
with diluent

10 mg*

FOR IV USE ONLY

***1 mg/mL when reconstituted with 10 mL of bacteriostatic water for injection, USP.**

10 vials lyophilized powder. 10 vials of bacteriostatic water for injection, USP.

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

When reconstituted with 10 mL of diluent (bacteriostatic water for injection, USP) the resultant solution will contain per mL:

vecuronium bromide	1 mg
citric acid anhydrous, USP	2.075 mg
sodium phosphate dibasic anhydrous, USP	1.625 mg
mannitol, USP (to adjust tonicity)	9.7 mg
benzyl alcohol (preservative)*	0.9%

May contain sodium hydroxide and/or phosphoric acid for pH adjustment. pH 4 (3.5 to 4.5).

* From supplied diluent

Usual Dosage: Read enclosed prescribing information.

Storage: Store dry powder at controlled room temperature 15° to 30°C (59° to 86°F).
PROTECT FROM LIGHT.
When reconstituted with bacteriostatic water for injection: **CONTAINS BENZYL ALCOHOL WHICH IS NOT FOR USE IN NEWBORNS. Use within 5 days. May be stored at room temperature or refrigerated.**
If reconstituted with sterile water for injection or other compatible I.V. solutions (per package insert): **Refrigerate vial. Use within 24 hours. Single use only.**
Discard unused portion.
Caution: Federal (USA) law prohibits dispensing without prescription.
WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

RAO5725-2/R2-1/98

Printed in USA

Exp.

Lot

(01) 1 030074 163401 2

10 vials, lyophilized powder

VECURONIUM BROMIDE FOR INJECTION

20 mg*

FOR IV USE ONLY

***1 mg/mL when reconstituted to 20 mL.**

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

10 Units/**NDC 0074-1634-01**

10 vials

VECURONIUM BROMIDE FOR INJECTION

20 mg* **FOR IV USE ONLY**

No Refrigeration Required

10 vials, lyophilized powder

10 Units/**NDC 0074-1634-01**

VECURONIUM BROMIDE FOR INJECTION

20 mg*

FOR IV USE ONLY

***1 mg/mL when reconstituted to 20 mL.**

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

When reconstituted with 20 mL of sterile water for injection the resultant solution will contain per mL:

vecuronium bromide	1 mg
citric acid anhydrous, USP	2.075 mg
sodium phosphate dibasic anhydrous, USP	1.625 mg
mannitol, USP (to adjust tonicity)	9.7 mg

May contain sodium hydroxide and/or phosphoric acid for pH adjustment. pH 4 (3.5 to 4.5).

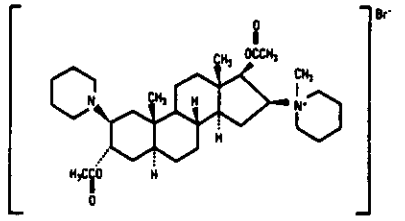
Usual Dosage: Read enclosed prescribing information.

VECURONIUM BROMIDE FOR INJECTION

THIS DRUG SHOULD BE ADMINISTERED BY ADEQUATELY TRAINED INDIVIDUALS FAMILIAR WITH ITS ACTIONS, CHARACTERISTICS, AND HAZARDS.

DESCRIPTION

Vecuronium bromide for injection is a nondepolarizing neuromuscular blocking agent of intermediate duration, chemically designated as piperidinium, 1-[(2β, 3α, 5α, 16β, 17β)-3, 17-bis (acetyloxy)-2-(1-piperidinyl) androstan-16-yl]-1-methyl-, bromide. Vecuronium bromide for injection is prepared as a solution and lyophilized in its final container. The structural formula is:



Its chemical formula is $C_{34}H_{57}BrN_2O_4$ with molecular weight 637.74.

Vecuronium bromide is supplied as a sterile nonpyrogenic freeze-dried buffered cake of very fine microscopic crystalline particles for intravenous injection only. Each 10 mL vial contains 10 mg vecuronium bromide, 20.75 mg citric acid anhydrous, 16.25 mg sodium phosphate dibasic anhydrous, 97 mg mannitol (to adjust tonicity), sodium hydroxide and/or phosphoric acid to buffer and adjust to a pH of 4 (3.5 to 4.5). Each 20 mL vial contains 20 mg of vecuronium bromide, 41.5 mg citric acid anhydrous, 32.5 mg sodium phosphate dibasic anhydrous, 194 mg mannitol (to adjust tonicity), sodium hydroxide and/or phosphoric acid to buffer and adjust to a pH of 4 (3.5 to 4.5). Bacteriostatic water for injection, USP when supplied contains 0.9% w/v BENZYL ALCOHOL, WHICH IS NOT FOR USE IN NEWBORNS.

CLINICAL PHARMACOLOGY

Vecuronium for injection is a nondepolarizing neuromuscular blocking agent possessing all of the characteristic pharmacological actions of this class of drugs (curariform). It acts by competing for cholinergic receptors at the motor end-plate. The antagonism to acetylcholine is inhibited and neuromuscular block is reversed by acetylcholinesterase inhibitors such as neostigmine, edrophonium, and pyridostigmine. Vecuronium is about 1/3 more potent than pancuronium; the duration of neuromuscular blockade produced by vecuronium bromide is shorter than that of pancuronium at initially equipotent doses. The time to onset of paralysis decreases and the duration of maximum effect increases with increasing vecuronium bromide doses. The use of a peripheral nerve stimulator is recommended in assessing the degree of muscular relaxation with all neuromuscular blocking drugs. The ED_{90} (dose required to produce 90% suppression of the muscle twitch response with balanced anesthesia) has averaged 0.057 mg/kg (0.049 to 0.062 mg/kg in various studies). An initial vecuronium bromide dose of 0.08 to 0.10 mg/kg generally produces first depression of twitch in approximately 1 minute, good or excellent intubation conditions within 2.5 to 3 minutes, and maximum neuromuscular blockade within 3 to 5 minutes of injection in most patients.

Under balanced anesthesia, the time to recovery to 25% of control (clinical duration) is approximately 25 to 40 minutes after injection and recovery is usually 95% complete approximately 45-65 minutes after injection of intubating dose. The neuromuscular blocking action of vecuronium is slightly enhanced in the presence of potent inhalation anesthetics. If vecuronium is first administered more than 5 minutes after the start of the

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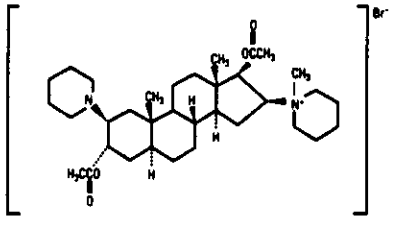

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Under balanced anesthesia, the time to recovery to 25% of control (clinical duration) is approximately 25 to 40 minutes after injection and recovery is usually 95% complete approximately 45-85 minutes after injection of intubating dose. The neuromuscular blocking action of vecuronium is slightly enhanced in the presence of potent inhalation anesthetics. If vecuronium is first administered more than 5 minutes after the start of the

reversed by acetylcholinesterase inhibitors such as neostigmine, edrophonium, and pyridostigmine. Vecuronium is about 1/3 more potent than pancuronium; the duration of neuromuscular blockade produced by vecuronium bromide is shorter than that of pancuronium at initially equipotent doses. The time to onset of paralysis decreases and the duration of maximum effect increases with increasing vecuronium bromide doses. The use of a peripheral nerve stimulator is recommended in assessing the degree of muscular relaxation with all neuromuscular blocking drugs. The ED_{90} (dose required to produce 90% suppression of the muscle twitch response with balanced anesthesia) has averaged 0.057 mg/kg (0.049 to 0.082 mg/kg in various studies). An initial vecuronium bromide dose of 0.08 to 0.10 mg/kg generally produces first depression of twitch in approximately 1 minute, good or excellent intubation conditions within 2.5 to 3 minutes, and maximum neuromuscular blockade within 3 to 5 minutes of injection in most patients.

Under balanced anesthesia, the time to recovery to 25% of control (clinical duration) is approximately 25 to 40 minutes after injection and recovery is usually 95% complete approximately 45-65 minutes after injection of intubating dose. The neuromuscular blocking action of vecuronium is slightly enhanced in the presence of potent inhalation anesthetics. If vecuronium is first administered more than 5 minutes after the start of the inhalation of enflurane, isoflurane, or halothane, or when steady state has been achieved, the intubating dose of vecuronium bromide may be decreased by approximately 15% (see **DOSAGE AND ADMINISTRATION** section). Prior administration of succinylcholine may enhance the neuromuscular blocking effect of vecuronium and its duration of action. With succinylcholine as the intubating agent, initial doses of 0.04-0.06 mg/kg of vecuronium will produce complete neuromuscular block with clinical duration of action of 25-30 minutes. If succinylcholine is used prior to vecuronium, the administration of vecuronium should be delayed until the patient starts recovering from succinylcholine-induced neuromuscular blockade. The effect of prior use of other nondepolarizing neuromuscular blocking agents on the activity of vecuronium has not been studied (see **PRECAUTIONS, Drug Interactions**).

Repeated administration of maintenance doses of vecuronium has little or no cumulative effect on the duration of neuromuscular blockade. Therefore, repeat doses can be administered at relatively regular intervals with predictable results. After an initial dose of 0.08 to 0.10 mg/kg under balanced anesthesia, the first maintenance dose (suggested maintenance dose is 0.010 to 0.015 mg/kg) is generally required within 25 to 40 minutes; subsequent maintenance doses, if required, may be administered at approximately 12 to 15 minute intervals. Halothane anesthesia increases the clinical duration of the maintenance dose only slightly. Under enflurane a maintenance dose of 0.010 mg/kg is approximately equal to 0.015 mg/kg dose under balanced anesthesia.

The recovery index (time from 25% to 75% recovery) is approximately 15-25 minutes under balanced or halothane anesthesia. When recovery from vecuronium neuromuscular blocking effect begins, it proceeds more rapidly than recovery from pancuronium. Once spontaneous recovery has started, the neuromuscular block produced by vecuronium is readily reversed with various anticholinesterase agents, e.g., pyridostigmine, neostigmine, or edrophonium in conjunction with an anticholinergic agent such as atropine or glycopyrrolate. Rapid recovery is a finding consistent with vecuronium short elimination half-life, although there have been occasional reports of prolonged neuromuscular blockade in patients in the intensive care unit (see **PRECAUTIONS**).

The administration of clinical doses of vecuronium bromide is not characterized by laboratory or clinical signs of chemically mediated histamine release. This does not preclude the possibility of rare hypersensitivity reactions (see **ADVERSE REACTIONS**).

Pharmacokinetics: At clinical doses of 0.04-0.10 mg/kg, 60-80% of vecuronium bromide is usually bound to plasma protein. The distribution half-life following a single intravenous dose (range 0.025-0.280 mg/kg) is approximately 4 minutes. Elimination half-life over this sample dosage range is approximately 65-75 minutes in healthy surgical patients and in renal failure patients undergoing transplant surgery.

In late pregnancy, elimination half-life may be shortened to approximately 35-40 minutes. The volume of distribution at steady state is approximately 300-400 mL/kg; systemic rate of clearance is approximately 3-4.5 mL/minute/kg. In man, urine recovery of vecuronium varies from 3-35% within 24 hours. Data derived from patients requiring insertion of a T-tube in the common bile duct suggests that 25-50% of a total intravenous dose of vecuronium may be excreted in bile within 42 hours. Only unchanged vecuronium has been detected in human plasma following use during surgery. In addition, one metabolite 3-desacetyl vecuronium has been rarely detected in human plasma following prolonged clinical use in the I.C.U. (See **PRECAUTIONS: Long Term Use in I.C.U.**). One metabolite, 3-desacetyl vecuronium has been recovered in the urine of some

short elimination half-life, although there have been occasional reports of prolonged neuromuscular blockade in patients in the intensive care unit (see **PRECAUTIONS**).

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This metabolite has been judged by animal screening (dogs and cats) to have 50% or more of the potency of vecuronium; equipotent doses are of approximately the same duration as vecuronium in dogs and cats. Biliary excretion accounts for about half the dose of vecuronium bromide within 7 hours in the anesthetized rat. Circulatory bypass of the liver (cat preparation) prolongs recovery from vecuronium. Limited data derived from patients with cirrhosis or cholestasis suggests that some measurements of recovery may be doubled in such patients. In patients with renal failure, measurements of recovery do not differ significantly from similar measurements in healthy patients.

Studies involving routine hemodynamic monitoring in good risk surgical patients reveal that the administration of vecuronium bromide in doses up to three times that needed to produce clinical relaxation (0.15 mg/kg) did not produce clinically significant changes in systolic, diastolic or mean arterial pressure. The heart rate, under similar monitoring, remained unchanged in some studies and was lowered by a mean of up to 8% in other studies. A large dose of 0.28 mg/kg administered during a period of no stimulation, while patients were being prepared for coronary artery bypass grafting was not associated with alterations in rate-pressure-product or pulmonary capillary wedge pressure. Systemic vascular resistance was lowered slightly and cardiac output was increased insignificantly. (The drug has not been studied in patients with hemodynamic dysfunction secondary to cardiac valvular disease). Limited clinical experience with use of vecuronium during the surgery for pheochromocytoma has shown that administration of this drug is not associated with changes in blood pressure or heart rate.

Unlike other nondepolarizing skeletal muscle relaxants, vecuronium has no clinically significant effects on hemodynamic parameters. Vecuronium will not counteract those hemodynamic changes or known side effects produced by or associated with anesthetic agents, other drugs or various other factors known to alter hemodynamics.

INDICATIONS AND USAGE

Vecuronium bromide is indicated as an adjunct to general anesthesia, to facilitate endotracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation.

CONTRAINDICATIONS

Vecuronium bromide is contraindicated in patients known to have a hypersensitivity to it.

WARNINGS

VECURONIUM BROMIDE SHOULD BE ADMINISTERED IN CAREFULLY ADJUSTED DOSAGE BY OR UNDER THE SUPERVISION OF EXPERIENCED CLINICIANS WHO ARE FAMILIAR WITH ITS ACTIONS AND THE POSSIBLE COMPLICATIONS THAT MIGHT OCCUR FOLLOWING ITS USE. THE DRUG SHOULD NOT BE ADMINISTERED UNLESS FACILITIES FOR INTUBATION, ARTIFICIAL RESPIRATION, OXYGEN THERAPY, AND REVERSAL AGENTS ARE IMMEDIATELY AVAILABLE. THE CLINICIAN MUST BE PREPARED TO ASSIST OR CONTROL RESPIRATION. TO REDUCE THE POSSIBILITY OF PROLONGED NEUROMUSCULAR BLOCKADE AND OTHER POSSIBLE COMPLICATIONS THAT MIGHT OCCUR FOLLOWING LONG-TERM USE IN THE ICU, VECURONIUM BROMIDE OR ANY OTHER NEUROMUSCULAR BLOCKING AGENT SHOULD BE ADMINISTERED IN CAREFULLY ADJUSTED DOSES BY OR UNDER THE SUPERVISION OF EXPERIENCED CLINICIANS WHO ARE FAMILIAR WITH ITS ACTIONS

develop symptoms consistent with tissue muscle atrophy. The recovery picture may vary from regaining movement and strength in all muscles to initial recovery of movement of the facial and small muscles of the extremities then to the remaining muscles. In rare cases recovery may be over an extended period of time and may even, on occasion, involve rehabilitation. Therefore, when there is a need for long-term mechanical ventilation, the benefits-to-risk ratio of neuromuscular blockade must be considered.

Continuous infusion or intermittent bolus dosing to support mechanical ventilation has not been studied sufficiently to support dosage recommendations. IN THE INTENSIVE CARE UNIT, APPROPRIATE MONITORING, WITH THE USE OF A PERIPHERAL NERVE STIMULATOR TO ASSESS THE DEGREE OF NEUROMUSCULAR BLOCKADE IS RECOMMENDED TO HELP PRECLUDE POSSIBLE PROLONGATION OF THE BLOCKADE. WHENEVER THE USE OF VECURONIUM OR ANY NEUROMUSCULAR BLOCKING AGENT IS CONTEMPLATED IN THE ICU, IT IS RECOMMENDED THAT NEUROMUSCULAR TRANSMISSION BE MONITORED CONTINUOUSLY DURING ADMINISTRATION AND RECOVERY WITH THE HELP OF A NERVE STIMULATOR. ADDITIONAL DOSES OF VECURONIUM BROMIDE OR ANY OTHER NEUROMUSCULAR BLOCKING AGENT SHOULD NOT BE GIVEN BEFORE THERE IS A DEFINITE RESPONSE TO T_1 OR TO THE FIRST TWITCH. IF NO RESPONSE IS ELICITED, INFUSION ADMINISTRATION SHOULD BE DISCONTINUED UNTIL A RESPONSE RETURNS.

Severe Obesity or Neuromuscular Disease: Patients with severe obesity or neuromuscular disease may pose airway and/or ventilatory problems requiring special care before, during and after the use of neuromuscular blocking agents such as vecuronium.

Malignant Hyperthermia: Many drugs used in anesthetic practice are suspected of being capable of triggering a potentially fatal hypermetabolism of skeletal muscle known as malignant hyperthermia. There are insufficient data derived from screening in susceptible animals (swine) to establish whether or not vecuronium is capable of triggering malignant hyperthermia.

C.N.S.: Vecuronium has no known effect on consciousness, the pain threshold or cerebration. Administration must be accompanied by adequate anesthesia or sedation.

Drug Interactions: Prior administration of succinylcholine may enhance the neuromuscular blocking effect of vecuronium for injection and its duration of action. If succinylcholine is used before vecuronium the administration of vecuronium should be delayed until the succinylcholine effect shows signs of wearing off. With succinylcholine as the intubating agent, initial doses of 0.04-0.06 mg/kg of vecuronium bromide may be administered to produce complete neuromuscular block with clinical duration of action of 25-30 minutes (see **CLINICAL PHARMACOLOGY**).

The use of vecuronium before succinylcholine, in order to attenuate some of the side effects of succinylcholine, has not been sufficiently studied.

Other nondepolarizing neuromuscular blocking agents

Side-by-side Label Copy Comparison
Carton Label
Vecuronium Bromide for Injection 10 mg/Vial with Bacteriostatic Water for Injection, USP Diluent
Abbott's original labeling is on top; our revised labeling is on the bottom

TOP PANEL

10 x 10 mL vials, powder and diluent

10 Units/**NDC 0074-1613-01**

VECURONIUM BROMIDE FOR INJECTION with diluent

10 mg*

FOR IV USE ONLY

***1 mg/mL** when reconstituted with **10 mL** of bacteriostatic water for injection, USP.

10 vials lyophilized powder.
10 vials of bacteriostatic water for injection, USP.

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

10 x 10 mL vials (powder)
10 x 10 mL vials (diluent)

10 Units/**NDC 0074-1613-01**

Revised to specify: "10 x 10 mL vials (powder) 10 x 10 mL vials (diluent)"

VECURONIUM BROMIDE FOR INJECTION with diluent

10 mg*

FOR IV USE ONLY

***1 mg/mL** when reconstituted with **10 mL** of bacteriostatic water for injection, USP.

10 vials lyophilized powder.
10 vials of bacteriostatic water for injection, USP.

WARNING: Vecuronium bromide may cause respiratory depression. Facilities for artificial respiration must be immediately available.

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

Changed from black to red ink to increase prominence.

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO: 4

2. ANDA 75-164

3. NAME AND ADDRESS OF APPLICANT
Abbott Laboratories
Attention: Jill N. Sackett
Hospital Products Division
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, IL 60064-3537

4. LEGAL BASIS FOR SUBMISSION
A patent certification statement claiming that Patents #4,237,126 and 4,297,351 are valid until 8/29/99 is appended. The RLD Norcuron™ is not entitled to a period of marketing exclusivity as per the 17th Edition of Approved Drug Products.

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Vecuronium Bromide for Injection

8. SUPPLEMENT PROVIDE FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm

June 30, 1997--	Original Submission
August 6, 1997--	Amendment
September 12, 1997--	New Correspondence
November 21, 1997--	New Correspondence
February 6, 1998 --	Major amendment
October 12, 1998-	Minor amendment
February 4, 1999 -	Telephone amendment to clarify postapproval testing
July 26, 1999 -	New Correspondence
September 13, 1999-	Amendment

FDA

July 25, 1997--	Refuse to file letter
September 5, 1997--	Acceptance letter to firm
December 10, 1997 --	Chemistry deficiency fax
December 31, 1997--	Bio granted waiver
January 6, 1998--	Label deficiency fax
July 14, 1998--	Methods validation results
July 21, 1998 --	Micro deficiency
September 2, 1998-	Label review acceptable
September 15, 1998-	Chemistry deficiency #2
September 15, 1998-	Bio review acceptable

February 4, 1999- Phone call by Chemist
July 16, 1999 GMP Deficiency letter

10. PHARMACOLOGICAL CATEGORY
Relaxant-Skeletal Muscle Relaxer

11. Rx or OTC
Rx

12. RELATED ANDAs/DMFs
, NDS

13. DOSAGE FORM
Lyophilized

14. POTENCY
10 mg/vial
20 mg/vial
10 mg/vial with
Bacteristatic Water for Injection

15. CHEMICAL NAME AND STRUCTURE
1-< 3, 17-Bis-acetyloxy)-2-(1-piperdinyl) androstan - 16-yl>-1-methylpiperidinium bromide

16. RECORDS AND REPORT:
EER acceptable, dated 9/20/99.
Bio waiver granted.
Methods validation completed, with minor changes to methods.
DMF is current and satisfactory.

17. COMMENTS
No outstanding Chemistry issues.

18. CONCLUSIONS AND RECOMMENDATIONS
ANDA recommended for approval.

19. REVIEWER:
Radhika Rajagopalan, Ph.D.

DATE COMPLETED:
October 4, 1999

Radhika Rajagopalan 10/7/99

Page(s) 1

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releasable.

Chemistry Review #4

10/4/99

Page(s) 2

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Chemistry Review

#3 P 9/15/88

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

BIOEQUIVALENCE REVIEW(S)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-164 APPLICANT: Abbott Laboratories

DRUG PRODUCT: Vecuronium Bromide for Injection 10mg/vial and 20 mg/vial

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-164 APPLICANT: Abbott Laboratories

DRUG PRODUCT: Vecuronium Bromide for Injection 10mg/vial and 20 mg/vial

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

Vecuronium Bromide for Injection
10 mg/Vial and 20 mg/Vial
ANDA #75-164
Reviewer: Moheb H. Makary
WP. 75164W.897

Abbott Laboratories
Abbott Park, Illinois
Submission Date:
August 6, 1997

Review of Waiver Requests

I. Objective:

The firm has requested waivers of bioequivalence study requirements for its products Vecuronium Bromide for Injection, 10 mg/Vial and 20 mg/Vial. Innovator products are Norcuron® for Injection 10 mg/Vial and 20 mg/Vial, manufactured by Organon Inc. Vecuronium Bromide for Injection is a nondepolarizing neuromuscular blocking agent of intermediate duration. It is supplied as a of very fine microscopic crystalline particles for intravenous injection only.

II. Formulations: **(Not to be released under FOI)**

The formulations of Abbott's Vecuronium Bromide and Organon's Norcuron® for Injection, 10 mg/Vial and 20 mg/Vial are shown in Table I.

Comments:

1. The active and inactive ingredients and their concentrations for the test products are the same as those of the innovator's Norcuron® for Injection 10 mg/vial and 20 mg/vial, manufactured by Organon Inc.

2. Waivers of in vivo bioequivalence study requirements may be granted based on 21 CFR 320.22(b)(1).

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Abbott Laboratories, demonstrates that Vecuronium Bromide for Injection, 10 mg/Vial and 20 mg/Vial fall under 21 CFR 320.22 (b)(1). The waivers of in vivo bioequivalence study for the test products are granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test injectable formulations 10 mg/Vial and 20 mg/Vial to be bioequivalent to Norcuron® Injectable, 10 mg/Vial and 20 mg/Vial, respectively, manufactured by Organon Inc.

The firm should be informed of the above recommendation.

Moheb H. Makary, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALLED RMHATRE
FT INITIALLED RMHATRE

/S/ Date: 12/12/97

Concur: Date: 12/31/97
Dale P. Conner
/S/
Director
Division of Bioequivalence

File.

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

MICROBIOLOGY REVIEW(S)

OFFICE OF GENERIC DRUGS, HFD-640
Microbiology Review #3
January 25, 1999

A. 1. **ANDA 75-164**

APPLICANT Abbott Labs
D-389 Bldg AP30
200 Abbott Park
Abbott Park IL 60064-3537

2. PRODUCT NAME: Vecuronium Bromide for Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 10 mg/vial in 10 mL vials and 20 mg/vials in 25 mL vials, 10 mg/vial in 10 mL vials with 10 mL Bacteriostatic Water For Injection USP [Diluent], Single Dose, Lyophilized Powder, Intravenous

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Neuromuscular Block

B. 1. DATE OF INITIAL SUBMISSION: (Originally Refuse-To-File)
Filing date: August 6, 1997
(Received August 6, 1997)

2. DATE OF FAX AMENDMENT: December 16, 1998
Subject of this Review (Received December 22, 1998)
3. RELATED DOCUMENTS: None
4. ASSIGNED FOR REVIEW: 1/25/99

C. REMARKS: The subject amendment provides for the response to the microbiology deficiencies in the facsimile letter dated November 18, 1998.

D. CONCLUSIONS: The submission is recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

/S/ 1/25/99
Andrea S. High, Ph. D.

Page(s) 1

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Micro Review #3

1/25/99

Microbiology Comments to be Provided to the Applicant

ANDA: 75-164 **APPLICANT: Abbott Labs**

DRUG PRODUCT: Vecuronium Bromide for Injection,
10 mg/vial and 20 mg/vial

A. Microbiology Deficiencies:

1. Please provide summaries to demonstrate that the rubber components do not contain detectable amounts of endotoxin when tested prior to washing as stated in your response.

2. Please provide sterilization validation summaries for the from the filling line to the

3. Your statement regarding leaking vials assumes the detection of leaking vials *prior* to the challenge and incubation. Please state the failure rate for the container/closure test <u>after</u> incubation.

4. Please specify the regardless of filtration. If the actual <u>storage time</u> is greater than 48 hours, studies to support prolonged storage should be provided.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

/S/ for

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS, HFD-640

Microbiology Review #2

October 26, 1998

A. 1. **ANDA 75-164**

APPLICANT Abbott Labs
D-389 Bldg AP30
200 Abbott Park
Abbott Park IL 60064-3537

2. PRODUCT NAME: Vecuronium Bromide for Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 10 mg/vial in 10 mL vials and 20 mg/vials in 25 mL vials, 10 mg/vial in 10 mL vials with 10 mL Bacteriostatic Water For Injection USP [Diluent], Single Dose, Lyophilized Powder, Intravenous

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Neuromuscular Block

B. 1. DATE OF INITIAL SUBMISSION: (Originally Refuse-To-File)
Filing date: August 6, 1997
Subject of this Review (Received August 6, 1997)

2. DATE OF AMENDMENT: August 21, 1998
Subject of this Review (Received August 25, 1998)

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: 10/26/98

C. REMARKS: The subject amendment provides for the response to the microbiology deficiency letter dated July 21, 1998.

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments regarding the filling on are provided in "E. Review Notes" and "Microbiology Comments to be Provided to the Applicant".

/S/ 10/27/98
Andrea S. High, Ph. D.

cc:

5-164a
F. Holcombe, Jr.

11/3/98

Page(s) 5

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Micro Review #2

10/27/98

OFFICE OF GENERIC DRUGS, HFD-640

Microbiology Review #1

July 16, 1998

A. 1. **ANDA 75-164**

APPLICANT Abbott Labs
D-389 Bldg AP30
200 Abbott Park
Abbott Park IL 60064-3537

2. PRODUCT NAME: Vecuronium Bromide for Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 10 mg/vial in 10 mL vials and 20 mg/vials in 25 mL vials, 10 mg/vial in 10 mL vials with 10 mL Bacteriostatic Water For Injection USP [Diluent], Single Dose, Lyophilized Powder, Intravenous

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Neuromuscular Block

B. 1. DATE OF INITIAL SUBMISSION: (Originally Refuse-To-File)
Filing date: August 6, 1997
Subject of this Review (Received August 6, 1997)

2. DATE OF AMENDMENT: August 6, 1997
Subject of this Review (Received August 8, 1997)

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: 7/10/98

C. REMARKS: The subject drug product is aseptically filled on [redacted] at the North Chicago pharmaceutical facility.

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments regarding the aseptic filling process/terminal sterilization are provided in "E. Review Notes" and "Microbiology Comments to be Provided to Applicant".

/S/ 7/16/98
Andrea S. High, Ph. D.

cc:

7/20/98
54
Holcombe, Jr.

Page(s) 10

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releasable.

Micro Review #1

7/10/95

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

ADMINISTRATIVE DOCUMENTS

RL
draft #1
10/4/99

DIVISION APPROVAL SUMMARY

ANDA: 75-164 **DRUG PRODUCT:** Vecuronium Bromide for Injection 10 mg/vial, 20 mg/vial and 10 mg/vial with Bacteriostatic Water for Injection

FIRM: Abbott Laboratories

DOSAGE: Lyophillized Powder

STRENGTH: 10 mg/vial, 20 mg/vial and 10 mg/vial with Bacteriostatic Water for Injection

CGMP STATEMENT/EIR UPDATE STATUS:

CGMP: Statement provided on 2-38.

EIR: EER acceptable on 9/20/99.

BIO STUDIES/BIOEQUIVALENCE STATUS:

Bio waiver granted on 12/31/97.

METHODS VALIDATION:

Field conducted methods validation and found them suitable. Results filed in volume 2.1.

STABILITY (conditions, containers and methods):

Bio batch was set up on stability in the proposed container/closure systems and data reported. The following are the firm's stability tests and specifications.

Test	Specifications
Vecuronium Bromide	
Physical Appearance	
Reconstitution time	
Identification	
Bacterial Endotoxins	
Sterility	

¬H		
ıoisture		
Mannitol		
Particulate Matter		
Related Substances		
Single Unknown		
Total		

LABELING REVIEW STATUS:
Acceptable dated 9/2/98.

STERILIZATION VALIDATION (If Applicable):
Satisfactory review dated 1/25/99.

BATCH SIZES:

Bio batch (identity #, drug substance source):
The drug substance is supplied by . The bio batch size is

STABILITY BATCH (different from bio batch, manu. Site, process):
Stability batch is the same as bio batch.

PROPOSED PRODUCTION BATCH:

Reprocessing statement is enclosed on page 3-330.

COMMENTS:
Approvable

CHEMISTRY REVIEWER: Radhika Rajagopalan, Ph.D.
DATE: 10/4/99

/S/
10/4/99

RECORD OF TELEPHONE CONVERSATION

I called of Abbott, Jean Conway about ANDA 75-164, their unapproved original for Vecuronium bromide for a clarification on post approval testing protocol. The firm indicated testing per protocol for the first three validation batches and then one lot to be tested annualy. I told them to modify it so one lot annualy will be tested at 0, 3, 6, 9, 12, 18, 24 and annualy thereafter at expiry. She will provide it as a telephone amendment.

DATE
2/4/99

ANDA NUMBER
75-164

IND NUMBER

TELECON

INITIATED BY **MADE**
APPLICANT/ SPONSOR X **BY TELE.**
X **FDA** _ **IN PERSON**

PRODUCT NAME
Vecuronium bromide for Inj.

FIRM NAME
Abbott Labs

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Jean Conaway
Reg. Affairs

TELEPHONE NUMBER
(847) 937-6845

SIGNATURE
R. Rajagopalan

x:\new\firmsam\abbott\tcons\75164feb.1

ISb 15/99.

TENTATIVE APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-164 Date of Submission: February 6, 1998

Applicant's Name: Abbott Laboratories

Established Name: Vecuronium Bromide for Injection, 10 mg/vial and 20 mg/vial

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: Vecuronium Bromide for Injection - 10 mg & 20 mg; Bacteriostatic Water for Injection, USP - 10 mL

Satisfactory in FPL as of 2/6/98 submission

Carton Labeling: 10 vials, lyophilized powder (10 mg & 20 mg); 10 x 10 mL vials (10 mg powder and diluent)

Satisfactory in FPL as of 2/6/98 submission

Professional Package Insert Labeling:

Satisfactory in FPL as of 2/6/98 submission

Auxiliary Labeling:

Satisfactory in FPL as of 2/6/98 submission

Revisions needed post-approval:

1. Replace "CAUTION: Federal.." statement with "Rx only" and relocate to the principal display panel.

2. Increase the space where pharmacist writes on container label.

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Norcuron® Injection

NDA Number: 18-776

NDA Drug Name: Norcuron® Injection

NDA Firm: Organon

Date of Approval of NDA Insert and supplement #: January 3, 1992/S-016

Has this been verified by the MIS system for the NDA?
Yes

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels and carton labeling:

a. The labeling of the listed drug NORCURON® (Organon, revised 12/91; approved 1/3/92).

b. Also used is the labeling of an approved generic Vecuronium Bromide Injection, ANDA 74-334 (August 3, 1995).

c. USP 23 for labeling guidance for Bacteriostatic Water for Injection.

FOR THE RECORD

1. MODEL LABELING

   a. This review was based upon the labeling of the listed drug NORCURON® (Organon, revised 12/91; approved 1/3/92).

   b. Also used is the labeling of an approved generic Vecuronium Bromide Injection, ANDA 74-334 (August 3, 1995).

   c. USP 23 for labeling guidance for Bacteriostatic Water for Injection.

2. Some of the recommendations made in this review based on the previous FTR for this drug found in the file folder. To be specific,

a. Comment (a)(iii) under CONTAINER: See FTR prepared by Shannon 9/1/93 and signed by JP 9/3/93.

b. Comment (a)(iv) under CONTAINER : See FTR prepared by Shannon 8/10/93 & signed by Yana Mille 8/10/93. Consequently, we will **not** ask the firm to add "Retain in carton until contents are used" on container labels and carton labeling.

3. One generic firm (Marsam) for the approved Vecuronium Injection (ANDA 73-334) argued that addition of the WARNING statement "WARNING: paralyzing Agent" to the labels and aluminum seal for vial cap is a stronger warning than "respiratory depression" and should be standard phrase for all containers of neuromuscular blocking agents. Therefore the firm had submitted this revision as a SSCBE on July 17, 1997. In fact, these identical warning statement appear on the cap for "Succinylcholine Injection by Abbott Laboratories (see the Marsam's supplemental application dated July 17, 1996 in vol.3.1 for ANDA 74-334 for detail). The agency has sent consult to NDA review division (HFD-170) regarding this proposal and received agreement from HFD-170 on this labeling change (see Medical Officer Consult dated 10/30/96 on 74-334/SL-001 in vol.3.1.). Consequently, the agency has approved this change (74-334/S-001) based on the consult outcome even though the innovator's labeling still is not approved for this change. However, since the NDA products still has not implemented on these changes, we will **not** ask for these changes to the applicant. (Decision made between Chan Park and John Grace, Team Leader).

4. INACTIVE INGREDIENTS

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 64 & 65 (Volume 1.1).

5. PATENTS/EXCLUSIVITIES

No entitlement to exclusivity.

Patent # 4237126 - August 20, 1999
Patent # 4297351 - August 20, 1999. The firm's statement is accurate.

6. The "description and solubility" of the drug products found in the DESCRIPTION section is identical with those described in the innovator's insert labeling.

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

NDA - Store dry powder at controlled room temperature 15°-30°C (59°-86°F). Protect from light.

ANDA - Store at controlled room temperature 15°-30°C (59°-86°F). Protect from light.

8. PACKAGING CONFIGURATIONS

NDA - 10 mg & 20 mg vials without BWFI.
10 mg vials with BWFI.

ANDA - 10 mg & 25 mg vials without BWFI
10 mg vials with BWFI.

9. CONTAINER/CLOSURE SYSTEM (Vecuronium Bromide for Injection)

10 mL & 25 mL Flint, Tubing vial type I (for 10 mg & 20 mg, respectively),

10 mg: West Stopper & Aluminum seal, Flipoff top, Red.
20 mg: West Stopper & Aluminum seal, Flipoff top, Blue.
(see P. 5-246 in vol.1.5)

10. We have encouraged the firm to enclose the "WARNING" statement in a box (preferably in red color) to increase the prominence. The firm has increased the prominence using a contrasting color (red for 10 mg, blue for 20 mg) matching other prominent information on the container and carton labeling. We note that the innovator has this "WARNING" statement in black ink without being enlarged nor enclosed in a box. We find the sponsor's proposal is acceptable.

Date of Review: August 27, 1998

Date of Submission: February 6, 1998

Cycle # 2 (FPL)

Primary Reviewer: Chan Park /S/ **Date:** 9/2/98

Team Leader: Charlie Hoppes /S/ **Date:** 9/3/98

---

cc:

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-164

CORRESPONDENCE

ABBOTT

9/20/99

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

ORIG AMENDMENT
N/Am

September 13, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS,
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

Via Fax 301-594-1174
(Paper Copy Via Federal Express)

Re: ANDA 75-164 Vecuronium Bromide for Injection (10mg/Vial & 20mg/Vial)
MINOR AMENDMENT

Abbott Laboratories hereby amends the above-referenced abbreviated new drug application for the subject drug. We are responding to the Agency's letter dated July 16, 1999. The Agency reiterated comments made by the FDA Chicago District concerning CGMP issues at the Abbott Laboratories manufacturing facility in North Chicago. We have been informed that the FDA Chicago District Officer has revised its early position and now recommends approval of this ANDA. We include a statement from a responsible company official stating that Abbott Laboratories has been informed of the ANDA approval recommendation. We Also attach a copy of written District approval of the site. Please see Exhibit I. Abbott Laboratories is not required to significantly revise its procedures, controls or practices.

We trust that this submission is complete and that the ANDA may now be approved. Please telephone at your earliest convenience if any additional information is needed.

Sincerely,

ABBOTT LABORATORIES

Thomas F. Willer

Thomas F. Willer, Ph.D.
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-6845
Fax: (847) 938-7867
Internet: WILLETF@hpd.abbott.com

TFW:tw

g:9-99f.tfw/50 - Attachment

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

NEW CORRESP
NC

July 26, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS,
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

NC

ATTENTION: Douglas Sporn
Director

Re: ANDA 75-164 Vecuronium Bromide for Injection (10mg/Vial & 20mg/Vial)

Abbott Laboratories hereby amends the above-referenced abbreviated new drug application for the subject drug product. We are responding to the Agency's letter dated July 16, 1999. The Agency commented that the Abbott Laboratories North Chicago manufacturing facility received an unsatisfactory inspection (February-May, 1999) concerning CGMP issues. Abbott Laboratories has participated in written and verbal discussions with FDA, Chicago District. We will meet in early August, 1999, and hopefully resolve all outstanding issues, if any, applicable to this ANDA. We will respond as requested with a certification that FDA, Chicago District, recommends approval of this application. We will designate that submission as a MINOR AMENDMENT. If significant changes are made that were referenced in this ANDA, then we will designate the response as a MAJOR AMENDMENT.

We look forward to early resolution of this inspection and rapid approval of the ANDA since all other issues have previously be resolved with OGD. Please contact me at your earliest convenience if additional information is needed.

Sincerely,

ABBOTT LABORATORIES

Thomas F. Willer

Thomas F. Willer, Ph.D.
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-6845
Fax: (847) 938-7867
Internet: WILLETF@hpd.abbott.com

TFW:tw

g:7-99f.tfw/53

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

February 4, 1999

NDA ORIG AMENDMENT
N / FA

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

FAX: R. Rajagopalan 301-443-3839

Re: ANDA 75-164 Vecuronium Bromide for Injection (10mg/Vial & 20mg/Vial)

TELEPHONE AMENDMENT

Abbott Laboratories hereby amends the above-referenced original new drug application for the subject drug product submitted June 30, 1997. We are responding to a telephone conference from Radhika Rajagopalan, OGD to Jean Conaway, Abbott Laboratories on February 4, 1999 concerning the need to revised the post approval commitments on the proposed stability protocols submitted.

REQUEST: **Please revise the post approval commitments to assure that the first three marketed lots, as well as, one lot annually are placed on the stability protocol and tested at the designated test intervals through the product expiration date.**

RESPONSE: Provided in EXHIBIT I are the proposed revised stability protocols which include the revisions as requested by the Agency.

We trust that this submission is complete and can be expeditiously approved. Please telephone me at your earliest convenience if I can provide additional information.

Sincerely,

ABBOTT LABORATORIES

Thomas F. Willer

Thomas F. Willer, Ph.D.
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-6845
Fax: (847) 938-7867
Internet: WILLETF@hpd.abbott.com

ABBOTT

Hospital Products Division
Abbott Laboratories
Dept. 389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

October 12, 1998

NEW CORRESP

NC

Encl # 99 [illegible] 25

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

FACSIMILE AMENDMENT
Chemistry, Manufacturing and Controls

RE: ANDA 75-164 Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial)

Abbott Laboratories herein responds to a September 15,1998, facsimile deficiency letter received from Kassandra Sherrod of the Agency. The letter contained deficiencies identified by the FDA laboratory conducting methods validation. We provide the following responses:

Page(s) 1

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Commercial/Confidential

Information and are not

releasable.

10/12/98

We trust that this information is complete.

Sincerely,

ABBOTT LABORATORIES

Jill N. Sackett
Assistant Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
Fax: (847) 938-7867
10-98fda

DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

DATE: 14 July 1998

FROM: Director, Science Branch
Philadelphia District, HFR-CE160

SUBJECT: **ANDA 75-164, Vercuronium Bromide for Injection, 10 mg/vial and 20 mg/vial**
Abbott Laboratories, North Chicago, IL 60064
RE: 98-785-370

TO: Radhika Rajagopalan, Review Chemist,
Office of Generic Drugs, CDER

The Philadelphia District Laboratory performed the analysis of Vercuronium Bromide for Injection, 10 mg/vial and 20 mg/vial, using the firm's method and samples provided. Attached are the summary of results, worksheets, and comments for the subject ANDA.

In evaluating the firm's methods, the following problems were encountered:

Based on the analytical results, the ANDA method appears to be suitable, but the following comments or problems stated above should be considered before approving the ANDA. No other problems were encountered with the analytical methods.

W. Charles Becoat

cc: HFR-CE100
HFD-300
HFC-140
HFR-CE150
Lab B: D. Lech
File

ABBOTT

Hospital Products Division
Abbott Laboratories
Dept. 389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

ORIG AMEND

February 6, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

MAJOR AMENDMENT
Chemistry, Manufacturing and Controls, Labeling

RE: ANDA 75-164 Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial)

Abbott Laboratories herein responds to December 10, 1997, and January 6, 1998, deficiency letters telefaxed by Kassandra Sherrod and Julia Johnson, respectively, of the Agency. The first letter contained chemistry, manufacturing and controls deficiencies while the second letter contained labeling deficiencies. We provide the following responses:

CHEMISTRY, MANUFACTURING AND CONTROLS
A. Deficiencies

Request 1: Please provide a COA for any in house reference standards used in

Page(s) 3

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releasable.

2/6/98

LABELING DEFICIENCIES

Revised final printed labeling is provided in Exhibit X. We have responded to the Agency's specific requests as detailed below. Additionally, to aid in review, we have provided in Exhibit XI a side-by-side comparison with the newly revised labeling and our last submitted labeling with all differences annotated and explained.

1. CONTAINER

a. Vecuronium Bromide for Injection - 10 mg & 20 mg

i. Delete the statements "10 mL vial" and "20 mL vial" from your labels. Please note that your proposed container for 20 mg drug product is "25 mL" rather than "20 mL".

Response: We have complied with this request and have revised the labeling accordingly.

ii. Some of the statements including "Contains benzyl...in newborns" on the 20 mg container labels is difficult to read, in particular the pale blue print on white background. Revise your container labels to increase the readability of these statements.

Response: We have complied with this request and have revised the labeling accordingly. We have selected a darker blue background for the subject text.

iii. Replace "By:" with "Time:" on a line for reconstitution with Bacteriostatic Water for Injection.

Response: We have complied with this request and have revised the labeling accordingly.

iv. Add the statement "PROTECT FROM LIGHT."

Response: We have complied with this request and have revised the labeling accordingly. We have deleted the term "Lyophilized Powder" from the container label to make room for this statement.

v. We encourage you to enclose the "WARNING" statement in a box (preferably in red color) to increase the prominence.

v. Response: We note that the innovator's container labels (original submission, page 1-13) print the warning statement in black ink and position the text *vertically* on the label. The text is not enlarged nor is it enclosed in a box. To increase the prominence as requested by the Agency and remain similar to the innovator, we have highlighted the warning statement in the contrasting color chosen for other prominent information on our container label (red for the 10 mg dose, blue for the 20 mg dose). Our text is positioned horizontally on the label, which enhances readability over vertically positioned text. We, like the innovator, do not enclose the statement in a box.

vi. Revise the statement "Dosage/...insert" to read as follows:

USUAL DOSAGE: See package insert.

Response: We note that our current container label copy matches that of the innovator: "**Dosage/Storage:** See package insert" (original submission, page 1-13). To more closely comply with the Agency's request and yet remain similar to the innovator, we have revised the statement to read "**Usual Dosage/Storage:** See package insert."

vii. We encourage you to include the following if space permits.

Store dry powder at controlled room temperature 15° - 30°C (59° - 86°F).

Response: Unfortunately, we lack the space to include this information on our container labels. We note that the innovator does not include this statement on their container labels (original submission, page 1-13). This information *is* present on our product carton and insert. Furthermore, our container label advises the user to consult the package insert for storage information (see item vi immediately above).

b. Bacteriostatic Water for Injection, USP - 10 mL

i. Increase the print size of the text "for Injection, USP"

Response: We have complied with this request and have revised the labeling accordingly.

ii. Relocate and/or revise the prominence of the statement "Not for use in Newborns". We refer you to the monograph for Bacteriostatic Water for Injection" in USP 23 for guidance.

Response: We have complied with this request and have revised the labeling accordingly per USP 23.

2. CARTON

a. 10 x 10 mL and 10 x 20 mL vials, lyophilized powder

i. Revise to read "10 vials, lyophilized powder" and "10 vials, lyophilized powder". Please note that your proposed container for 20 mg drug product is "25 mL" rather than "20 mL".

Response: We have complied with this request and have revised the labeling accordingly.

ii. See (a) (v) under CONTAINER.

Response: Response: We note that the innovator's carton labels (original submission, pages 1-14 through 1-19) print the warning statement in black ink. The text is not enlarged nor is it enclosed in a box. To increase the prominence as requested by the Agency and remain similar to the innovator, we have highlighted the warning statement in the contrasting color chosen for other prominent information on the our carton label (red for the 10 mg dose, blue for the 20 mg dose). We, like the innovator, do not enclose the statement in a box.

iii. Increase the prominence of the text "Protect from light".

Response: We have complied with this request and have revised the labeling accordingly.

iv. We encourage you to revise the storage requirement to read "Store dry powder at controlled room temperature 15° - 30°C (59° - 86°F)."

Response: We have complied with this request and have revised the labeling accordingly.

v. "USUAL DOSAGE:..." rather than "DOSAGE:".

Response: We have complied with this request and have revised the labeling accordingly. We have retained our upper/lower case format which matches that used by the innovator.

vi. We encourage you revise the paragraph beginning "If reconstituted..." to read:

...compatible I.V. solutions (per package insert): Refrigerate...

Response: We have complied with this request and have revised the labeling accordingly.

b. 10 x 10 mL vials, powder and diluent

i. Revise the net quantity statement to read:

10 x 10 mL vials (powder)
10 x 10 mL vials (diluent)

Response: We have complied with this request and have revised the labeling accordingly.

ii. See comments (a) (ii) through (vi) under CARTON.

Response: See responses for (a) (ii) through (vi) under CARTON.

3. AUXILIARY LABEL

Add "Time mixed:_____" following "Date mixed:_____By:_____"

Response: We have complied with this request and have revised the labeling accordingly. Some of the text was rearranged to accommodate the added phrase.

4. INSERT

a. CLINICAL PHARMACOLOGY

i. Replace "vecuronium bromide" with "vecuronium" throughout the text except when referring to the dose of vecuronium bromide.

Response: We have complied with this request and have revised the labeling accordingly.

ii. Second paragraph, last sentence

(see PRECAUTIONS, Drug Interactions)

Response: We have complied with this request and have revised the labeling accordingly.

iii. Pharmacokinetics - Second paragraph, last sentence:

One metabolite, 3-desacetyl vecuronium has been recovered...

Response: We have complied with this request and have revised the labeling accordingly.

b. PRECAUTIONS

i. See comment (i) under CLINICAL PHARMACOLOGY.

Response: We have complied with this request and have revised the labeling accordingly.

ii. Hepatic Disease:

...(see CLINICAL PHARMACOLOGY, Pharmacokinetics).

Response: We have complied with this request and have revised the labeling accordingly.

c. ADVERSE REACTIONS

Replace "vecuronium bromide" with "vecuronium" throughout the text.

Response: We have complied with this request and have revised the labeling accordingly.

d. OVERDOSAGE

See comment under ADVERSE REACTIONS.

Response: We have complied with this request and have revised the labeling accordingly.

e. DOSAGE AND ADMINISTRATION

i. Use "mcg" rather than "μg" when referring to micrograms.

Response: We have complied with this request and have revised the labeling accordingly.

ii. Use by continuous infusion - Paragraph 5
(Infusion solutions of vecuronium...)

Response: We have complied with this request and have revised the labeling accordingly.

Revise to read as follows:

...solutions such as Dextrose Injection 5%, Sodium Chloride Injection 0.9%, Dextrose (5%) and Sodium Chloride Injection, or Lactated Ringer's Injection.

Response: We have complied with this request and have revised the labeling accordingly.

iii. Dosage in Pediatric Patients - Paragraph 1, sentence 1:

Older pediatric patients...

Response: We have complied with this request and have revised the labeling accordingly.

iv. Compatibility - Revise to read as follows:

Vecuronium bromide is compatible in solution with:
Sodium Chloride Injection 0.9%
Dextrose Injection 5%
Sterile Water for Injection
Dextrose (5%) and Sodium Chloride Injection
Lactated Ringer's Injection.
Use...

Response: We have complied with this request and have revised the labeling accordingly.

f. HOW SUPPLIED

i. Store dry powder at controlled...

Response: We have complied with this request and have revised the labeling accordingly.

ii. After Reconstitution:

We encourage you to relocate this subsection to the compatibility subsection under DOSAGE AND ADMINISTRATION section immediately following the sentence "Use within 24 hours..."

Response: We have complied with this request and have revised the labeling accordingly.

We trust that this information is complete.

Sincerely,
ABBOTT LABORATORIES

Jill N. Sackett
Assistant Director, Regulatory Affairs
Hospital Products Division
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ABBOTT

Hospital Products Division
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Abbott Park, Illinois 60064-3537

FDA ORIG AMENDMENT
A 2

November 21, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

Minor Amendment
RE: ANDA 75-164 Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial)

Abbott Laboratories wishes to the amend the above referenced application to correct an entry in the manufacturing instructions for the subject drug and to provide updated stability data for the exhibit batches.

On page 2-48 and page 6-243 of the original application, step 2 of "Filling/Initial Stoppering" incorrectly gives a target fill volume of 2.58 mL. The target fill volume should be 5.15 mL. Corrected pages are provided in Exhibit I.

Additional stability data, now collected through 9 months, 25°C and 30°C, and 6 months 40°C, are provided in the stability report in Exhibit II.

Sincerely,

ABBOTT LABORATORIES

Jill N. Sackett
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Hospital Products Division
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Page(s) 2

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Chemistry Review

#38 12/10/97

ABBOTT

Hospital Products Division
Abbott Laboratories
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200 Abbott Park Road
Abbott Park, Illinois 60064-3537

September 12, 1997

Correspondence.
10/14/97

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

NEW CORRESP

ATTENTION: Douglas Sporn
Director

RE: Vecuronium Bromide for Injection, 10 mg and 20 mg

On August 29, 1997, Abbott Laboratories submitted the above abbreviated new drug application for Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. The dosage forms and manufacturing site are as follows:

List Number	Dosage Form	Manufacturing Facility
1632	10 mg/10 mL Vial	
1634	20 mg/20 mL Vial	
1613	10 mg/10 mL Vial w/ 10 mL Bacteriostatic Water for Injection, USP	

On September 10, 1997, we received a telephone call from Peter Rickman of the Agency. Mr. Rickman explained that he was refusing to file this application, citing 21 CFR 314.101(d)(8) and stating that we had already filed ANDA 75-164, dated June 30, 1997, for the same dosage forms for our North Chicago manufacturing facility. He advised that one of these two ANDAs must be withdrawn.

We herein withdraw our ANDA dated August 29, 1997 for the . manufacturing facility. We apologize for any inconvenience this may have caused, and request that the review of ANDA 75-164 proceed expeditiously.

Sincerely,
ABBOTT LABORATORIES

J Sackett

Jill N. Sackett
Assistant Director, Regulatory Affairs
Hospital Products Division
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ABBOTT

Hospital Products Division
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Abbott Park, Illinois 60064-3537

NEW CORRESP

August 6, 1997

N 2

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

RE: ANDA 75-164 Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial)

The above application, dated June 30, 1997, included stability data for two lots of product as follows:

List Number	Concentration	Lot Number	Batch Size
1634	20 mg / 25 mL vial	22-890-JE	
1632	10 mg / 10 mL vial	22-889-JE	

Accountability sheets for Lot Nos. 22-890-JE and 22-889-JE are provided in Attachment I for quick reference.

Abbott Laboratories received a refusal-to-file letter from the Agency dated July 25, 1997. The letter stated:

> "You are required to completely package your exhibit batch in the containers proposed for marketing. For further reference, please refer to the letters to industry from the Director, Office of Generic Drugs, dated November 8, 1991, and August 4, 1993, and the February 8, 1995, Office of Generic Drugs Policy and Procedure Guide #41-95."

We provide the following explanation:

Our typical batch size for the 20 mg dosage form is planned to be Our typical batch size for the 10 mg dosage form is planned to be In support of the ANDA submission, a master batch was manufactured and used to fill both 20 mg and 10 mg vials.

Unfortunately, the commodity prep area misunderstood the planned batch size for this run. Accordingly, they prepared and provided an insufficient quantity of glass vials. Due to the shortage of glass vials, of solution remained at the completion of filling.

This is detailed on the accountability sheets provided in Attachment I. For Lot 22-889-JE, . of the master batch prepared as Lot 22-890-JE were used to fill the 10 mg vial and no solution was left over. The remaining solution was used to fill the 20 mg vials as Lot 22-890-JE. Here were left over. Thus only of the master batch were consumed in the manufacturing and filling process.

Please note that the master batch was also utilized to perform mix time validation. Results from the mix time validation confirmed that a homogenous solution was achieved and maintained during the manufacturing process.

Nonetheless, we herein amend the application to correct our typical batch size to or the 20 mg vial, based upon the *actual* amount of solution that was filled from the master batch. The typical batch size for the 10 mg vial remains at

Sincerely,

ABBOTT LABORATORIES

Jill N. Sackett
Assistant Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
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ANDA 75-164

Abbott Laboratories
Hospital Products Division
Attention: Jill N. Sackett
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, IL 60064-3537

JUL 25 1997

Dear Madam:

Please refer to your abbreviated new drug application dated June 30, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Vecuronium Bromide for Injection, 10 mg/vial and 20 mg/vial.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

> Your are required to completely package your exhibit batch in the containers proposed for marketing. For further reference, please refer to the letters to industry from the Director, Office of Generic Drugs, dated November 8, 1991, and August 4, 1993, and the February 8, 1995, Office of Generic Drugs Policy and Procedure Guide #41-95.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Anna Marie H. Weikel
Project Manager
(301) 827-5862

Sincerely yours,

/S/

Jerry Phillips 7/24/97
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

En

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

Refuse to File
Anna Marie H. Weikel
7/23/97

June 30, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

RE: ANDA Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial)

ORIGINAL ABBREVIATED NEW DRUG APPLICATION

Abbott Laboratories hereby submits an abbreviated new drug application for Vecuronium Bromide for Injection, (10 mg/vial and 20 mg/vial) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. The dosage form and manufacturing site may be described as follows:

List Number	Dosage Form	Manufacturing Facility
1632	10 mg/10 mL Vial	North Chicago, IL
1634	20 mg/25 mL Vial	North Chicago, IL
1613	10 mg/10 mL Vial w/ 10 mL Bacteriostatic Water for Injection, USP	North Chicago, IL

The basis for this submission is Vecuronium Bromide for Injection which is currently manufactured in the same dosage forms by Organon, Inc., West Orange, New Jersey, under the trade name Norcuron®. The NDA for this product is 18-776, approved April 30, 1984 (10 mg vial) and January 3, 1992 (20 mg vial).

Please refer to the accompanying Table of Contents for a list of the data supporting this submission. These data have been presented in six volumes consistent with the Office of Generic Drugs Policy and Procedure Guide #30-91 dated 4/10/91, entitled "Organization of an Abbreviated New Drug Application and an Abbreviated Antibiotic Application."

Abbott Laboratories will manufacture the finished dosage form at its currently approved North Chicago, Illinois facility. Certain portions of North Chicago, Illinois' Drug Master File ... have been reproduced here for ease of review. However, please refer to Drug Master File for a *full* description of this facility.

In compliance with 21 CFR 314 covering FDA pre approval inspections of manufacturing sites, Abbott Laboratories has submitted a complete copy of the CMC section from this application ("designated as the field copy") to the Chicago FDA district office with inspection responsibilities for the Abbott Laboratories manufacturing site listed in this application.

We also include in Section XXI of this application the "Certification Requirement of All applications For Approval of a Drug Product," as required by the Generic Drug Enforcement Act of 1992.

The sterilization assurance information is found in Section XI, Manufacturing and Processing Instructions section of this submission.

The convenience package, List 1613, is comprised of Vecuronium Bromide for Injection, 10 mg/vial, List 1632, with Bacteriostatic Water for Injection, USP, 10 mL Vial, List 3977, as a diluent. All data provided in this submission for Vecuronium Bromide for Injection, 10 mg/vial, List 1632, are also supportive of the convenience package, List 1613. List 3977 has been marketed by Abbott Laboratories as a grandfathered product for quite some time. In support of the diluent component, we provide draft labeling in Section V and marketed product stability data in Section XVII.4.

We request twenty-four (24) months expiration dating for these products based on the accelerated stability data enclosed. At the request of the Agency, we will provide samples of the drug substance and finished dosage form.

We trust that this submission is complete.

Sincerely,

Jill N. Sackett
Assistant Director, Regulatory Affairs
Hospital Products Division
Phone (847) 937-4085
Fax (847) 938-7867
vecur.doc

ANDA 75-164

Abbott Laboratories
Hospital Products Division
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, IL 60064-3537

SEP 5 1997

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to our "Refuse to File" letter dated July 25, 1997, and your amendment dated August 6, 1997.

NAME OF DRUG: Vecuronium Bromide for Injection, 10 mg/vial and 20 mg/vial

DATE OF APPLICATION: June 30, 1997

DATE OF RECEIPT: July 3, 1997

DATE ACCEPTABLE FOR FILING: August 8, 1997

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Kassandra Sherrod
Project Manager
(301) 827-5849

Sincerely yours,

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

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4/97