CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 075293Orig1s014

Trade Name:

Generic or Proper Name: midazolam hydrochloride injection

Sponsor: Hospira, Inc.

Approval Date: 05/20/2012

Indications:

Midazolam hydrochloride injection is indicated:

- intramuscularly or intravenously for preoperative sedation/anxiolysis/amnesia;

- intravenously as an agent for sedation/anxiolysis/amnesia prior to or during diagnostic, therapeutic or endoscopic procedures, such as bronchoscopy, gastroscopy, cystoscopy, coronary angiography, cardiac catheterization, oncology procedures, radiologic procedures, suture of lacerations and other procedures either alone or in combination with other CNS depressants;

(continued on next page)

(Indications - continued from prior page)

- intravenously for induction of general anesthesia, before administration of other anesthetic agents. With the use of narcotic premedication, induction of anesthesia can be attained within a relatively narrow dose range and in a short period of time. Intravenous midazolam can also be used as a component of intravenous supplementation of nitrous oxide and oxygen (balanced anesthesia);

- continuous intravenous infusion for sedation of intubated and mechanically ventilated patients as a component of anesthesia or during treatment in a critical care setting.

Midazolam is associated with a high incidence of partial or complete impairment or recall for the next several hours.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075293Orig1s014

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075293Orig1s014

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA# See Attached List

Hospira, Inc.
Attention: Judith Zutkis
Dept 0389, H2-2
275 N. Field Drive
Lake Forest, IL 60045-5046

Dear Madam:

This is in reference to your supplemental new drug applications dated June 03, 2011, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug applications in the attached list.

The supplemental applications, submitted as "Prior Approval Supplement", provide for an alternative source of API for use in the manufacture of final drug product.

We have completed the review of your supplemental applications and they are approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

ATTACHMENT LIST

ANDA	Drug Product and Strength
75293/S-014	Midazolam Hydrochloride Injection, 1 mg base/mL and 5 mg base/mL (Fliptop Vials)
75856/S-008	Midazolam Hydrochloride Injection (Preservative Free), 1 mg base/mL and 5 mg base/mL (Carpuject®)
75857/S-011	Midazolam Hydrochloride Injection (Preservative Free), 1 mg base/mL and 5 mg base/mL (Fliptop Vials)

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

/s/

VILAYAT A SAYEED
05/20/2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075293Orig1s014

CHEMISTRY REVIEW(S)

Office of Generic Drugs
Chemistry, Manufacturing, and Controls Review

Review # 01

ANDA# **75293/S-014** Midazolam Hydrochloride Injection, 1 mg base/mL and 5 mg base/mL (Fliptop Vials),
75856/S-008 Midazolam Hydrochloride Injection (Preservative Free), 1 mg base/mL and 5 mg base/mL (Carpuject®),
75857/S-011 Midazolam Hydrochloride Injection (Preservative Free), 1 mg base/mL and 5 mg base/mL (Fliptop Vials),

Name and Address of Applicant:

Applicant	***USA Agent***
Hospira, Inc. 275 North Field Dr. Dept. 0389, Bldg. H2-2 Lake Forest, IL 60045 Tel: 224-212-4949 Fax: 224-212-5401 Contact: Judith Zutkis, Director, Regulatory Affairs *Manufacturing facility*: **Hospira, Inc.** Highway 301 North Rocky Mount, NC 27801 Registration # 1021343	N/A

Purpose of Supplement
This bundle *Prior Approval Supplements*, provide for an alternative source of API (b) (4) to be used in the manufacture of final drug product, Midazolam Hydrochloride Injection, USP 1 mg/mL and 5 mg/mL.

Date(s) of Submission(s):
Supplemental submission: 06-03-2011

Pharmacological Category
Anesthetic

Trade Name
N/A

Nonproprietary Name
Midazolam HCl Injection USP

Dosage Form
Injectable

Potency
1 mg/mL and 5 mg/mL

Rx or OTC
Rx

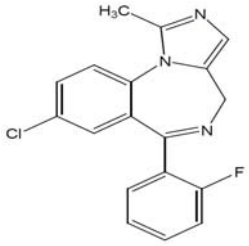
Samples
N/A

Related IND/NDA/DMF
(b) (4) (Adequate per review cycle # 7)

Sterilization
(b) (4)

Route of Administration
Injection (I.V.)

Chemical Name and Structure:
8-chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazole [1,5-a][1,4]benzodiazepine:



Molecular Formula: $C_{18}H_{13}ClFN_3$
Molecular Weight: 325.78
CAS Number: 59467-70-8

Remarks and Conclusion: ***Approvable***

This supplement is ***approvable*** due to no CMC deficiencies.

Recalls	**Reviewer**	**Date Completed**
N/A	Md Ashequr Rahman, Ph.D.	04-19-2012

Endorsements:
HFD-630/Md Ashequr Rahman, Ph.D., Review Chemist/5-9-2012
HFD-630/Laxma R Nagavelli, Ph.D., Team Leader/4/26/2012; 5/11/2012
HFD-630/Leigh Ann Sears, Project Manager/5/15/2012

Reviewer Notes

Labeling: *N/A*

Bioequivalency Status: *N/A*

Establishment Inspection: *Acceptable as of 7-25-2011*

Components/Composition/Manufacturing/Controls: *Satisfactory*

This prior supplemental application provides for an alternative source of API to be used in the manufacture of finished drug product, Midazolam Hydrochloride Injection, USP

The newly proposed API manufacturer is [redacted] (b) (4). The currently approved source of API, Midazolam USP is [redacted] (b) (4)

An alternative source of drug substance, Midazolam, USP manufactured by [redacted] (b) (4) is proposed for the manufacture of Midazolam Hydrochloride Injection USP 1 mg/mL and 5 mg/mL. The applicant states that the residual solvents and chromatographic limits are revised to be in line with [redacted] (b) (4) material and ICH guidelines. The limits for [redacted] (b) (4)

For each ANDA, one batch of the 5 mg/mL presentation of Midazolam Hydrochloride Injection was manufactured using the new source of API and placed on long term and accelerated stability studies per ICH guidelines. The mentioned strength was chosen to evaluate the effect of the proposed API changes on the drug product since the drug substance vendor is the only change compared to the currently approved drug product and this will represent the product that will exhibit the largest stopper surface to fill volume ratio. Hence, this strategy can be considered to represent a worst case stability scenario.

The applicant has submitted 03 months stability data at room temperature and accelerated conditions and based on the stability data generated, Hospira proposes 24 months expiration dating when stored at controlled room temperature ((20-25°C; 68-77°F). Hospira also commits to place the first commercial lot of each presentation under each ANDA onto commercial product stability.

The applicant states that the finished product manufacturing and controls, the components and composition, manufacturing process, container closure system, and expiration dating for the drug product will be the same as in the approved ANDAs. The following changes are proposed in this supplement.

In order to determine the effect of the proposed drug substance on the quality attributes of the drug product, Midazolam Hydrochloride Injection USP 5 mg/mL strength was manufactured and evaluated for the quality parameters including stability data through 3 months. The strength for the study was selected on the following basis:

1. This strength will exhibit the largest stopper surface to fill volume ratio.
2. 1 mg strength is proportionally similar (Step down formula) to the 5mg.
4. Manufacturing process of all the strengths is exactly same.
5. Similar CCS will be used.
6. This is injectable preparation and the similar excipients and quantity will be used
7. The composition and components are same.
5. The results of the ANDA batches of all the strengths demonstrate that all the strengths behave similarly with respect to all the quality parameters viz. release results and stability results.

Comparative drug substance specification between the currently approved and propose source of API and USP and EP specifications.

Table 3: Specification Comparison, USP, EP, Current Supplier and New Supplier

(b) (4)

[redacted]

8 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

Table 1. Site Establishment Information

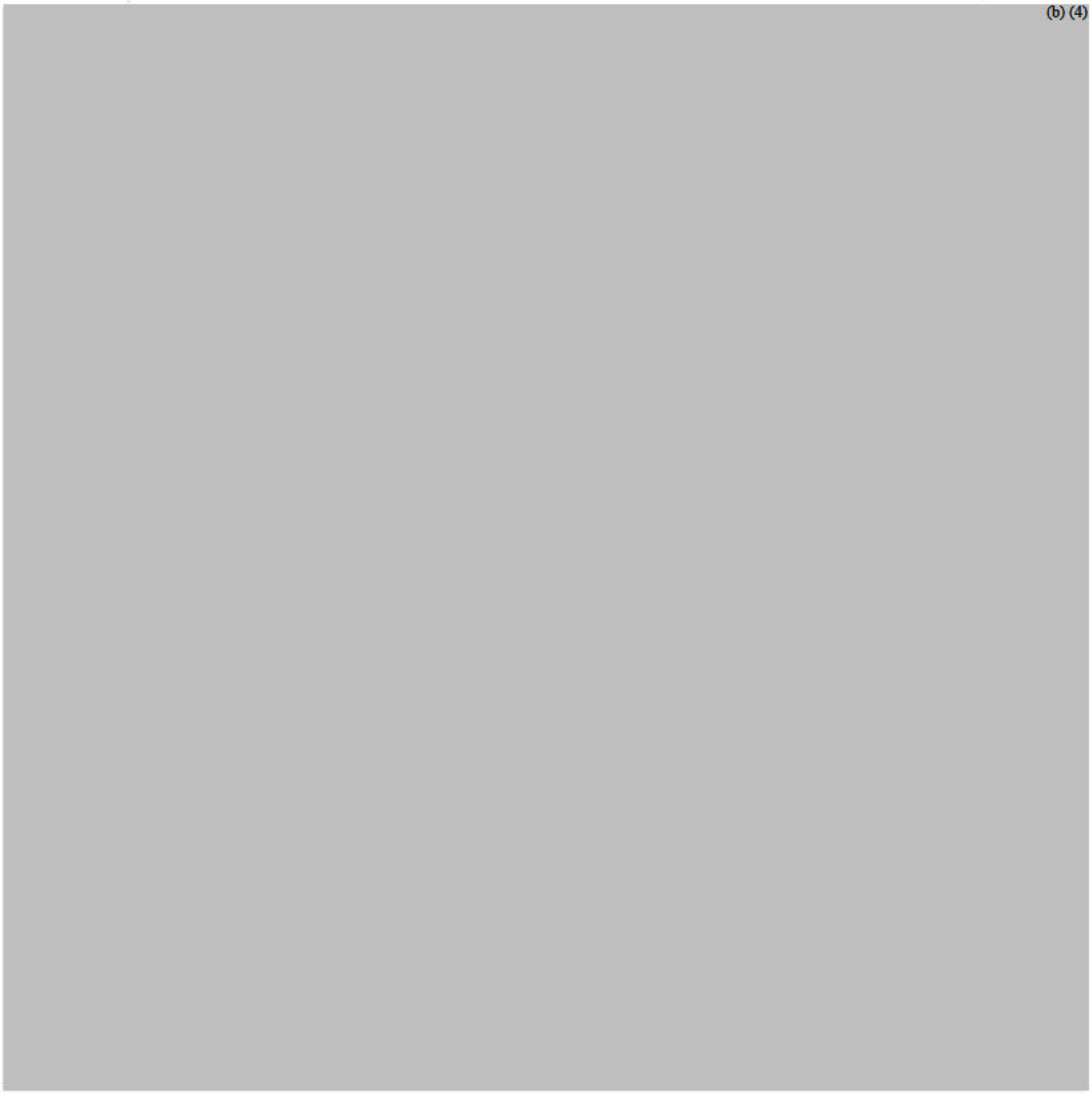
Company Name and Address	Contact Name	Responsibilities
Hospira, Inc. Highway 301 North Rocky Mount, NC 27801 Registration No. 1021343	Hector Jimenez Manager, Plant Quality Assurance Tel. (252) 977-5606 Fax (252) 977-5880 Email: hector.jimenez@hospira.com	Drug Substance testing Excipient testing Component testing In-process control testing Manufacture of drug product Release testing of drug product Packaging and labeling of drug product
Hospira, Inc. 375 North Field Drive Lake Forest, IL 60045 Registration No. 3004591926	Gary Moulton Manager, Quality Assurance Tel. (224) 212-4892 Fax. (224) 212-5205 Email: gary.moulton@hospira.com	Stability testing site for the drug product
		(b) (4)

[redacted]

Evaluation: Satisfactory

The manufacturer information for the drug product has been provided by the ANDA applicant. All the facilities mentioned above are listed in the EES. The new API source, (b) (4) is also included in the EES.

4 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page



Example stability data:

Table 2. Shelf Life Specifications

Test	Acceptance Criteria	Regulatory Analytical Procedure
Clarity	(b) (4)	Visual
Color		(b) (4)
Identification (HPLC)		USP Monograph
Assay		USP Monograph
Benzyl Alcohol		USP Monograph
(b) (4)		(b) (4)
Midazolam Related Substances Individual Known Impurity Individual Unknown Impurity Total Impurities		USP Monograph
Total Sodium		(b) (4)
Edetate Disodium (b) (4)		(b) (4)
Particulate Matter		USP <788>
pH		USP <791>
Sterility (Maintenance of Sterility)		(b) (4)
Bacterial Endotoxin		USP <85>

HPLC = High Performance liquid chromatography; NMT = Not more than

Three months room temperature stability data for Midazolam Hydrochloride Injection, USP 5 mg/mL (Batch# 10-105-DK packaged in fliptop glass vials):

Product:	Midazolam Hydrochloride Injection, USP	Container:	(b) (4)
Strength:	5 mg/mL	Closure:	
Batch No.:	10-105-DK	Seal:	
Product Filling Date:	24-Sept-2010	Time Zero Date:	19-Nov -2010

25°C / 40% Relative Humidity; Inverted

Test	Specification	Initial	3 months	6 months	9 months	12 months	18 months	24 months
	(b) (4)							
Clarity		Pass	Pass					
Color(APHA unit)		3	8					
Assay		100%	100%					
Benzyl Alcohol		101%	NR		NR			
(b) (4)		(b) (4)	(b) (4)		(b) (4)			
Midazolam Related Substances Individual Know Impurity Individual Unknown Impurity Total Impurities			(b) (4)					
Total Sodium		100%	NR	NR	NR	NR	NR	
Edetate Disodium (b) (4)		102%	NR		NR			
Particulate Matter		0 0	NR	NR	NR		NR	NR
pH		3.1	3.0					
Sterility (Maintenance of Sterility)		Pass	NR	NR	NR		NR	
Bacterial Endotoxin		(b) (4)	(b) (4)					

ND: None Detected.
NR: Not Required

Three months ACC stability data for Midazolam Hydrochloride Injection, USP 5 mg/mL (Batch# 10-105-DK packaged in fliptop glass vials):

Product:	Midazolam Hydrochloride Injection, USP	Container:	(b) (4)
Strength:	5 mg/mL	Closure:	
Batch No.:	10-105-DK	Seal:	
Product Filling Date:	24-Sept-2010	Time Zero Date:	19-Nov -2010

40°C / 25% Relative Humidity

Test	Specification	1 months	2 months	3months		6months	
		Inverted	Inverted	Inverted	Upright	Inverted	Upright
Clarity	(b) (4)	Pass	Pass	Pass	Pass		
Color (APHA unit)		8	9	11	11		
Assay		101%	100%	99%	99%		
Benzyl Alcohol		NR	NR	99%	100 %		
(b) (4)					(b) (4)		
Midazolam Related Substances Individual Know Impurity Individual Unknown Impurity Total Impurities					(b) (4)		
Total Sodium		NR	NR	100%	100%		
Edetate Disodium (b) (4)		NR	NR	99%	98 %		
Particulate Matter		NR	NR	5 1	4 0		
pH		3.1	3.0	3.0	3.0		
Sterility (Maintenance of Sterility)		NR	NR	Meet Require ment.	Meet Require ment.		
Bacterial Endotoxin					(b) (4)		

ND: None Detected.
NR: Not Required

Three months accelerated and up to three months room temperature stability data are provided for 5 mg strengths packaged in the existing container/closure system. All data are well within the specifications.

3.2.P.8.2.2 Post-Approval Stability Commitment

(b) (4)

Hospira commits to perform post-approval stability studies as outlined in the above marketed product stability protocol as approved by the Agency and report the results of the stability studies as they become available.

(b) (4)

Proposed Expiration Dating
Based on the data generated for Midazolam Hydrochloride Injection, USP 5 mg/mL stability batches, Hospira proposes conditional **24-months** expiration dating based on the available data. This dating will be verified by 24-months room temperature data, which will be filed annually as they become available, as per our commitment.

Comment:
The firm has proposed a new API supplier for drug product, Midazolam Hydrochloride Injection, USP 1 mg/mL and 5 mg/mL. Firm's proposed drug substance specification is in conformance with the USP monograph. The DMF cited for this source of API is currently adequate and the applicant's DS specifications is consistent with the DMF holder's specifications The formulation of drug product and manufacturing process and controls of drug product remain unchanged. The impurity profile of the drug substance from the new source by the ANDA applicant is proposed based on the USP monograph. The residual solvents in the drug substance are controlled per USP<467> and DMF holder recommendation. The drug product manufactured using the new API is comparable to that manufactured using the approved API in terms of quality and potency. Therefore, this supplement is found to be approvable.

This supplement is ***approvable*** due to no CMC deficiencies with the drug substance.

Packaging: *(see above review)*

Stability: *(see above review)*

Order of Review:

The application submission(s) covered by this review was taken in the date order or receipt:

Yes	No	X
: _____	: _____	

OFFICE OF GENERIC DRUGS EXPEDITED REVIEW REQUESTED

ANDA/SUPPLEMENT #:
75856/s-008, 75857/s-11 and
75293/s-14
DRUG: Midazolam Injection
PAS provides for alternate API from
(b) (4)

APPLICANT: Hospira
DATE OF SUBMISSION: 6-3-2011

The Office of Generic Drugs MaPP # 5240.1 lists the following criteria for granting expedited review status to a supplemental abbreviated new drug application. At least one of the criteria must be met.

1. PUBLIC HEALTH NEED. Events that affect the availability of a drug for which there is no alternative. (National drug shortage)

SPOT? Yes: _____ No: X _____

If yes, complete a SPOT form

DMF CHECKLIST FOR ANDA # 75-293/S-014, 75-856/S-08, 75-857/S-011

REVIEW # 01

DMF #	TYPE	HOLDER	ITEM REFERENCED	ACTION CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Active Ingredient	1	*Adequate*	5-9-2012	By Md Ashequr Rahman

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 – Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

ANDA# See Attached List

Hospira, Inc.
Attention: Judith Zutkis
Dept 0389, H2-2
275 N. Field Drive
Lake Forest, IL 60045-5046

Dear Madam:

This is in reference to your supplemental new drug applications dated June 03, 2011, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug applications for the attached list.

The supplemental applications, submitted as "Prior Approval Supplement", provide for an alternative source of API for use in the manufacture of final drug product.

We have completed the review of your supplemental applications and they are approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

ATTACHMENT LIST

ANDA	DRUG PRODUCT AND STRENGTH
75293/S-014	Midazolam Hydrochloride Injection, 1 mg base/mL and 5 mg base/mL (Fliptop Vials)
75856/S-008	Midazolam Hydrochloride Injection (Preservative Free), 1 mg base/mL and 5 mg base/mL (Carpuject®)
75857/S-011	Midazolam Hydrochloride Injection (Preservative Free), 1 mg base/mL and 5 mg base/mL (Fliptop Vials)

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/s/

MD A RAHMAN
05/16/2012

LAXMA R NAGAVELLI
05/16/2012

LEIGH A SEARS
05/16/2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075293Orig1s014

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

July 01, 2011

ANDA:
075293/S-014 (Lead) Midazolam Hydrochloride Injection
075856/S-008 Midazolam Hydrochloride Injection
075857/S-011 Midazolam Hydrochloride Injection

Drug Product Name
Proprietary: N/A
Non-proprietary: Midazolam Hydrochloride Injection

Drug Product Classification: N/A

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
06/03/2011	06/03/2011	N/A	06/28/2011

Submission History: None

Applicant/Sponsor
Name: Hospira, Inc.
Address: 275 North Field Dr.Dept. 0389,
Bldg. H2-2,Lake Forest, IL 60045
Representative: Judith Zutkis
Telephone: 224 212 4949

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: The submission **is recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: PAS Supplement

2. SUBMISSION PROVIDES FOR: Alternate API source ((b) (4) API)

3. MANUFACTURING SITE: Hospira, Inc. Highway 301 North, Rocky Mount, NC 27801

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Various

5. METHOD(S) OF STERILIZATION: Unchanged; (b) (4)

6. PHARMACOLOGICAL CATEGORY: sedative

B. SUPPORTING/RELATED DOCUMENTS: 75-856.doc, 03/05/2001, M. Stevens-Riley

C. REMARKS: This application has been submitted electronically. No comparability protocols included with this submission. The ANDA holder proposes eliminating the specification for API bioburden in this Prior Approval Supplement. The submissions are not grouped as a global submission in DARRTS; this reviewer has grouped the submissions as all indicate the identical proposed change.

filename: 075293s14.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability

The submission is **recommended** for approval on the basis of sterility assurance.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable –

N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology-

The bulk drug solution is (b) (4)

B. Brief Description of Microbiology Deficiencies –

None identified.

C. Assessment of Risk Due to Microbiology Deficiencies

No microbiology deficiencies were identified. The applicant demonstrates an adequate level of sterility assurance for the manufacturing process.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Microbiologist /Steven P. Donald, M.S.
Microbiology Team Leader / CDR Paul Dexter, M.S.

C. CC Block

cc: Field Copy

Product Quality Microbiology Assessment

The ANDA holder proposes to eliminate the specification for bioburden in the [redacted] as this is not requirement according to the USP monograph for Midazolam. The proposed drug substance includes an endotoxin limit of [redacted] There are no changes to the current specifications for the drug product: endotoxin, [redacted] and sterility, "meets the requirement". Batch analysis of exhibit lot PDO-256, manufactured with the proposed alternate API, shows an endotoxin result of [redacted] and a sterility result of "meets the requirements".

On June 30, 2011, this reviewer contacted Judith Zutkis, Regularory Affairs, Hospira, Inc. asking for information to indicate the manufacturing process has maintained a state of microbial control with the inclusion of the API from the proposed alternate supplier, [redacted] The request was answered by Colin Davis of Hospira, who provided [redacted] bioburden information from the bulk drug product manufactured with the API from the proposed, new source:

ANDA 75-856: Lot PDO-256 [redacted]
ANDA 75-857: Lot 10-104-DK; [redacted]
ANDA 75-293: Lot 10-105-DK; [redacted]

The review by M. Stevens-Riley 75-856.doc, 03/05/2001, indicates a bulk drug [redacted] bioburden alert level of [redacted]. The applicant states that the proposed drug substance vendor is the only proposed change, and that the finished product manufacturing and controls will remain unchanged.

The [redacted] bioburden limit is provided in the original review by M. Steven-Riley and the applicant indicates that the controls for the finished drug product will remain unchanged. This reviewer finds the proposed change acceptable.

This submission includes three-month stability data at room temperature and three-month stability data at accelerated conditions. Hospira proposes that the currently approved expiration dating be maintained: 24 months when stored at controlled room temperature (20-25°C; 68-77°F). [redacted]

Acceptable

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

/s/

STEVEN P DONALD
07/20/2011

KUN SHEN
07/29/2011

PAUL L DEXTER
08/15/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075293Orig1s014

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

OFFICE OF GENERIC DRUGS EXPEDITED REVIEW REQUESTED

ANDA/SUPPLEMENT #:
75856/s-008, 75857/s-11 and
75293/s-14
DRUG: Midazolam Injection
PAS provides for alternate API from
(b) (4)

APPLICANT: Hospira
DATE OF SUBMISSION: 6-3-2011

The Office of Generic Drugs MaPP # 5240.1 lists the following criteria for granting expedited review status to a supplemental abbreviated new drug application. At least one of the criteria must be met.

1. PUBLIC HEALTH NEED. Events that affect the availability of a drug for which there is no alternative. (National drug shortage)

2. EXTRAORDINARY HARDSHIP ON THE APPLICANT.

   a) Catastrophic events such as explosion, fire storms damage.

   b) Events that could not have been reasonably foreseen and for which the applicant could not plan. Examples include:

      - Abrupt discontinuation of supply of active ingredient, packaging material, or container closure; and
      - Relocation of a facility or change in an existing facility because of a catastrophic event (see item 2.a)

3. AGENCY NEED.
   a) Matters regarding the government's drug purchase program, upon request from the appropriate FDA office.
   b) Federal or state legal/regulatory actions, including mandated formation changes or labeling changes if it is in the Agency's best interest.
   c) Expiration-date extension or packaging change when the drug product is the subject of a government contract award.
   d) Request for approval of a strength that was previously tentatively approved (To be used in those cases where 180-day generic drug exclusivity prevented full approval of all strengths).

RECOMMENDATIONS:

DISCIPLINE	STATUS	SIGNATURE/DATE
Team Project Manager (PM must Endorse)	Grant x Deny☐	Simon Eng
Chemistry Team Leader (sign as needed)	Grant☐ Deny☐	
Micro Team Leader (sign as needed)	Grant☐ Deny☐	
Labeling Team Leader (sign as needed)	Grant☐ Deny☐	
Chem. Div./Deputy Director (DO must Endorse)	Grant☐ Deny☐	

RETURN TO PROJECT MANAGER CHEMISTRY TEAM: SELECT TEAM #
a) When expedited review is denied, notify the applicant by telephone
DATE

ENTER FORM INTO DFS

From: Sayeed, Vilayat A
Sent: Wednesday, April 18, 2012 4:39 PM
To: Eng, Simon
Subject: RE: Midazolam Shortage/request for expedited review of 75856/s-008, 75857/s-11 and 75293/s-14

No problem, file in DARRTS and I will sign the expedite request

Vilayat A. Sayeed, Ph.D.
Director, Division of Chemistry III
FDA/CDER/OPS/OGD
7500 Standish Place
MPN II Rockville, MD 20855
Office (240) 276-8486, fax (240) 276-8474
Vilayat.Sayeed@FDA.HHS.GOV

From: Eng, Simon
Sent: Wednesday, April 18, 2012 4:34 PM
To: Sayeed, Vilayat A
Subject: FW: Midazolam Shortage/request for expedited review of 75856/s-008, 75857/s-11 and 75293/s-14

Hello Dr. Sayeed,
Can you endorse this request by replying to my email? I will copy your response and paste to the supp expedited review request form for Bob and Harvey to sign next week.

This is a critical drug for sedation/anxiolysis/amnesia prior to surgical procedures and is in national drug shortage.

I just check the EER for 75856/s-008, 75857/s-11 and 75293/s-14, they are all acceptable.
These supps are for the same drug in different dosage forms, firm wanted to use (b) (4) as an alternate API.
Leigh Ann had assigned the review to MD Rahman on 3-28-12.

Thanks,
Simon

From: Eng, Simon
Sent: Wednesday, April 18, 2012 3:37 PM

To: Patel, Paras M; Greenberg, Harvey A
Cc: Rickman, William P; Ames, Timothy W
Subject: Midazolam Shortage/request for expedited review of 75856/s-008, 75857/s-11 and 75293/s-14

Hi Paras,
Harvey and Bob are on annual leave. They will be back next week.
75856/s-008, 75857/s-11 and 75293/s-14 were not granted expedited review status. I will prepare the supplement expedited review request for Harvey, Bob and the chem. Div director's endorsement. I will let you know when Bob signs off the expedited form next week.
Thanks,
Simon

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

/s/

SIMON S ENG
04/18/2012

VILAYAT A SAYEED
04/19/2012

WILLIAM P RICKMAN
04/19/2012