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APPLICATION NUMBER:

209260Orig1s000

NON-CLINICAL REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY NDA/BLA REVIEW AND EVALUATION

Application number:	209260
Supporting document/s:	eCTD
Applicant's letter date:	3/28/17
CDER stamp date:	3/28/17
Product:	Atropine Sulfate Ansyr™ Plastic Syringe
Indication:	for temporary blockade of severe or life threatening muscarinic effects
Applicant:	Fresenius Kabi USA, LLC
Review Division:	DCRP
Reviewer:	William T. Link, Ph.D.
Supervisor/Team Leader:	Albert DeFelice, Ph.D.
Division Director:	Norman Stockbridge, M.D., Ph.D.
Project Manager:	Sabry Soukehal

Template Version: September 1, 2010

Disclaimer

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Fresenius Kabi, USA, LLC (FK USA) is submitting this New Drug Application in accordance with Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355) to seek marketing clearance for Atropine Sulfate Injection, USP, 0.4 mg/mL in a 20 mL multi-dose glass vial.

The Reference Listed Drug (RLD), NDA 021146, Atropine Sulfate Ansyr™ Plastic Syringe, 0.1 mg/mL is manufactured by Hospira, Inc.

Strength	0.4 mg/mL			
Packaging Configuration	(b) (4) mL fill in a 20 mL vial			
Vial	20 mL, (b) (4) glass vial			
Stopper	20 mm , (b) (4) stopper			
Seal	20 mm, Flip-cap Aluminum crimp seal			
Drug Product Name	**Content (per mL)**	**Content (per vial)**	**Function**	**Quality of Ingredient**
Atropine sulfate monohydrate[1]	0.4 mg	8 mg	Active Ingredient	USP
Sodium Chloride	9 mg	180 mg	Tonicity adjuster	USP
Benzyl Alcohol	9 mg	180 mg	Preservative	NF
Sulfuric Acid[2]	QS	QS	pH Adjustor	NF
Water for Injection	QS to mL	QS to 20 mL	(b) (4)	USP

The inactive ingredients of the proposed drug product are the same as that of the reference listed drug except the addition of the preservative benzyl alcohol and sulfuric acid as the only pH adjuster to Fresenius Kabi USA, LLC (FK USA) drug product formulation.

Formulation Comparison Between Proposed Drug and RLD

Ingredients	**RLD**	**Proposed Drug Product**	**Function of Ingredients**
	Atropine Sulfate Ansyr™ Plastic Syringe	**Atropine Sulfate Injection, USP**	
Atropine sulfate monohydrate	0.1 mg/mL	0.4 mg/mL	Active pharmaceutical ingredient
Sodium Chloride, USP	9 mg/mL	9 mg/mL	Tonicity adjuster
Benzyl Alcohol, NF	N/A	9 mg/mL	Preservative
Sulfuric Acid, NF	q.s	q.s	pH adjuster
Sodium Hydroxide, NF	q.s	N/A	pH adjuster

Water for Injection, USP	q.s.	q.s	(b) (4)

The drug substance of the proposed drug product is Atropine Sulfate, USP, which is the same as that of the RLD Atropine Sulfate Ansyr™ Plastic Syringe. No properties or physical chemical characteristics of the drug substance were identified that affected drug product development, manufacturing, or performance.

All excipients used in the manufacture of FK USA's product meet the requirements of the current USP/NF including current USP< (b) (4) > for (b) (4) .

1.2 Brief Discussion of Nonclinical Findings

No new preclinical studies were submitted.

The only concern of this reviewer is the addition of the benzyl alcohol to the drug product and the resultant risk in the pediatric population. These concerns are adequately described in the Package Insert under ***5 Warnings and Precautions***.

1.3 Recommendations

1.3.1 Approvability

The product is approvable.

1.3.2 Additional Non Clinical Recommendations

none

1.3.3 Labeling

No changes recommended.

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/s/

WILLIAM T LINK
12/14/2017

ALBERT F DEFELICE
12/14/2017