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APPLICATION NUMBER:

206610Orig1s000

CLINICAL PHARMACOLOGY REVIEW(S)

CLINICAL PHARMACOLOGY REVIEW

NDA: 206610	Submission Date(s): 5/3/2014
Brand Name	Acetaminophen Injection
Generic Name	Acetaminophen Injection
Clinical Pharmacology Reviewer	Srikanth C. Nallani, Ph.D.
Team Leader	Yun Xu, Ph.D.
OCP Division	Division of Clinical Pharmacology II
OND Division	Anesthesia, Analgesia and Addiction Products
Sponsor	(b) (4)
Relevant IND(s)	NA
Submission Type	505(b)(2)
Formulation; Strength(s)	Lyophilized Powder for Injection; 1 gm/vial.
Indication	Relief of pain and fever.
Proposed Dosage Regimen	Administered every 4 – 6 hours.

Agila Specialities Pvt Ltd submitted a 505(b)(2) NDA application for approval of acetaminophen lyophilized powder for injection with reference to safety and efficacy established previously in an approved NDA 022450 Ofirmev (Reference drug).

QTPP Elements		Target	Justification
Dosage form		Lyophilized injection	505 (b)(2) approach, change in dosage form
Dosage strength		1 g/vial (10 mg/mL after reconstitution)	Pharmaceutical and therapeutic equivalent requirement - same strength (1000 mg/100 mL) as RLD after reconstitution.
Dose		4g/day	Pharmaceutical and therapeutic equivalent requirement - same dose
Route of administration		IV infusion	Pharmaceutical and therapeutic equivalent requirement - same route of administration as that of RLD
Pharmacokinetics		Similar as RLD	Bioequivalence requirement - Should have similar to RLD after reconstitution
Stability		At least 24-month shelf-life at room temperature	Equivalent to or better than liquid RLD shelf-life
Drug product quality attributes	Description	White to off-white lyophilized powder or cake filled in flint vial with lyo rubber stopper and aluminum seal.	
	Identification by HPLC	By HPLC- The retention time of the major peak in the chromatogram of the standard preparation should correspond to that of the retention time of the main peak in sample preparation, as obtained in the test for assay.	
	Identification by TLC	By TLC – The principal spot in the chromatogram obtained with sample preparation should correspond to that in the chromatogram obtained with the standard preparation.	
	Reconstitution time	NMT (b) (4) minutes	
	Uniformity of dosage units	The acceptance value of 10 dosage units should be less than or equal to (b) (4)% [L1 is (b) (4)%]	

There is no Clinical Pharmacology Data in the NDA. The sponsor has submitted biowaiver request and the ONDQA Biopharm team agreed to biowaiver for IV product (Note biowaiver memo by Dr. Kelly Kitchens dated 8/27/2014).

Labeling: The proposed product label is identical to Ofirmev product label. It is noteworthy that Ofirmev product label was recently updated.

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/s/

SRIKANTH C NALLANI
02/03/2015

YUN XU
02/03/2015