OFFICE OF CLINICAL PHARMACOLOGY ADDENDUM REVIEW

NDA: 202022 (S-8, SDN 217)	Original Submission Date: February 27, 2015
Brand Name	Edurant
Generic Name	Rilpivirine
Reviewer	Stanley Au, Pharm.D., BCPS
Pharmacometrics Team Leader	Jeffry Florian, Ph.D.
Clinical Pharmacology Team Leader	Shirley Seo, Ph.D.
OCP Division	Division of Clinical Pharmacology 4
OND Division	Division of Antiviral Products (DAVP)
Applicant	Janssen Research and Development
Formulation; strength(s)	Rilpivirine tablets (25 mg)
Indication	Treatment of HIV-1 infection
Review Type	Postmarketing requirement (PMR) submission: pediatric supplement

This is an addendum review to the primary Clinical Pharmacology Review entered into DARRTS for NDA 202022, S-8, SDN 217. This addendum for the primary Clinical Pharmacology Review updates the rilpivirine population pharmacokinetic parameters for adolescents in the rilpivirine U.S. prescribing information which were described on page 5 of the initial primary review. In the initial review, the population PK parameters were revised to exclude the rilpivirine plasma samples with Z isomer ratios that exceeded 10%; in addition, one subject (Subject 2130042) was excluded from the PK parameter summary because of uncertainty regarding the specific sample with a Z isomer ratio that exceeded 10% that was described as "Retest OTH / Day 1". Subsequently, the applicant provided a clarification that the sample in question from Subject 2130042 was not included in the original population PK analysis because information regarding the sampling time was not available (please see Labeling PMR/PMC Discussion Comments; DARRTS date August 13th, 2015 by Sohail Mosaddegh). The applicant also clarified that the methodology used to derive PK parameters for the analysis that excluded samples with Z isomers greater than 10% involved taking the median of an individual's PK parameter across all visits and then summarizing those individual median values to generate the summary population PK parameters. While not explicitly stated, based on reviewing the population PK analysis data, the applicant's revised rilpivirine PK parameters were derived to only include samples up to the week 48 visit. Based on this updated information, the Clinical Pharmacology review team agrees that subject 2130042 can be included in the analysis excluding the week 48, day 1 sample and also agrees with the applicant's methodology for calculating the rilpivirine population PK parameters in adolescents. The applicant's revised rilpivirine PK parameters in adolescents that are displayed below under "Final labeling". have been independently verified by the Clinical Pharmacology review team, and we concur with their inclusion in the rilpivirine U.S. prescribing information.

Labeling Recommendations

Applicant original labeling	Final labeling
Section 12 **Table (b) (4) Population Pharmacokinetic Estimates of Rilpivirine 25 mg once daily in Antiretroviral Treatment-Naïve HIV-1-Infected (b) (4) Subjects (b) (4) (Data from Phase (b) (4) Trial through Week 48)**	Section 12 **Table (b) (4) Population Pharmacokinetic Estimates of Rilpivirine 25 mg once daily in Antiretroviral Treatment-Naïve HIV-1-Infected (b) (4) Subjects (b) (4) (Data from Phase (b) (4) Trial through Week 48)**

Parameter	**Rilpivirine 25 mg once daily** **N = (b) (4)**
AUC_{24h} (ng•h/mL)	(b) (4)
Mean ± Standard Deviation	
Median (Range)	
C_{0h} (ng/mL)	
Mean ± Standard Deviation	
Median (Range)	

Parameter	**Rilpivirine 25 mg once daily** **N = (b) (4)**
AUC_{24h} (ng•h/mL)	(b) (4)
Mean ± Standard Deviation	
Median (Range)	
C_{0h} (ng/mL)	
Mean ± Standard Deviation	
Median (Range)	

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/s/

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08/21/2015

STANLEY AU
08/21/2015

SHIRLEY K SEO
08/24/2015