Clinical Pharmacology/Biopharmaceutics Review
BPCA Summary Review

PRODUCT (Generic Name):	Risperidone
PRODUCT (Brand Name):	Risperdal
DOSAGE FORM:	Tablets
DOSAGE STRENGTHS:	0.25mg, 0.5mg, 1 mg, 2mg, 3mg, and 4 mg
NDA:	20-272/20588
NDA TYPE:	Supplement for **Schizophrenia** and Bipolar disorder in children and adolescents in response to FDA Pediatric Written Request Letter
SUBMISSION DATE:	December 22, 2006
SPONSOR:	Johnson and Johnson
OND DIVISION:	HFD

EXECUTIVE SUMMARY

Risperidal is currently indicated in the treatment of schizophrenia or bipolar I in adults. It has been believed that the pharmacokinetics of Risperidal in children (less than 12 years), adolescents (12 to 17 years) and adults, are similar. Results from the current population pharmacokinetic analysis indicates that the pharmacokinetics are similar after correction for body weight. However there was no dose response for efficacy. Therefore no dose adjustments based on body weight are warranted in children and adolescents (between 10-17 years) for schizophrenia or bipolar I disorder.

This sNDA includes a meta analysis of several population pharmacokinetic studies done in children and adolescents with several different titrated dosage regimens based upon either once-a-day or twice-a-day maximum tolerated dose or maximum tolerated dose/kg/day. Targeted titrated maximum tolerated doses ranged from 0.5mg/day to 6

mg/day while dose titrations based upon weight ranged between 0.007 to 0.12 mg/kg/day.

The population pharmacokinetic study was done in 472 children and adolescents patients, ages 6-18 (studies ris,-bim-301, ris-usa-231, ris-usa-160) . Study durations were from 12-21 days.

The overall conclusions from the pharmacokinetic studies in adolescents and children were:

- The exposure in children and adolescents was similar based upon mg/kg body weight.
- A dose response relationship was not observed for the schizophrenia study in adolescents or for the bipolar I study in children/adolescents.
- No dose adjustments based on body weight are warranted in children and adolescents (between 10-17 years).

RECOMMENDATION

From a Clinical Pharmacology/Biopharmaceutics perspective this sNDA is acceptable with the labeling changes suggested by the reviewer.

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/s/

Raman Baweja
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