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APPROVAL PACKAGE FOR:

**APPLICATION NUMBER
20-641/SE5-007**

Pharmacology Review(s)

**HFD-570 :- DIVISION OF PULMONARY AND ALLERGY DRUG PRODUCTS
REVIEW AND EVALUATION OF PHARMACOLOGY AND TOXICOLOGY DATA
Labeling Review**

NDA No. 20-641 SE5-007

Submission Date: 24 NOV 1999

Reviewer: Timothy J. McGovern, Ph.D.

Review Completed: 20 SEP 2000

Information to be Conveyed to Sponsor: Yes (✓), No ()

Sponsor: Schering Corporation

Drug Name: *Generic:* Loratadine *Commercial:* Claritin Syrup™

Drug Class: Anti-histamine

Route of Administration: Oral inhalation

Background: The sponsor submitted a pediatric labeling supplement to the NDA in response to the Official Written Request for pediatric studies dated October 15, 1998. The sponsor submitted pharmacokinetic and safety studies required for pediatric subjects 2 to 5 years of age. Claritin Syrup is currently indicated for ages 6 and older with a recommended dose of 10 mg/day. The supplement proposes a recommended dose of 5 mg for ages 2 to 5 years old.

The following sections of the proposed label should be revised as follows to include information relevant to the younger :

Exposure ratio data for children should be added to the "Carcinogenesis, Mutagenesis, Impairment of Fertility:" . Clinical study C97-033 (5 mg syrup in pediatrics 2-5 years old) demonstrated an AUC(0-t) of 16.7 ng*hr/ml loratadine and 87.2 ng*hr/ml desloratadine (Table 1).

Table 1. Comparative pharmacokinetic data for loratadine.

Species	Dose	Loratadine AUC (ng*hr/ml)	Exposure ratio*	Desloratadine AUC (ng*hr/ml)	Exposure ratio*
Human (2-5 yrs old) ^a	5 mg syrup	16.7	-	87.2	-
Mouse ^b	40 mg/kg, diet	85.3	5.1	1860.7	21.3
Rat ^c	25 mg/kg, diet	679	40.7	7017	80.4
	10 mg/kg, diet	269	16.1	1619	18.6

a: Study C97-033

*: mouse or rat AUC divided by human AUC.

b: Study D-25201: 28 day PK study

c: Study D-25200: 28 day PK study

Based upon the exposure ratios listed in Table 1, the first paragraph of this section should read as follows:

1 pages redacted from this section of
the approval package consisted of draft labeling

OVERDOSAGE: In adults, somnolence, tachycardia, and headache have been...
Treatment of overdosage would reasonably....

RECOMMENDATIONS

1. The proposed labeling submitted by the sponsor is acceptable, with incorporation of the suggested revisions for the labeling sections entitled Carcinogenesis, Mutagenesis, Impairment of Fertility, and OVERDOSAGE as indicated above.

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/S/

Timothy J. McGovern, Ph.D., Pharmacologist
/S/ *9/20/00*
Sept 20, 2000

Drug: **Claritin Syrup**

	age	# daily		mg/day	kg	mg/kg	factor	mg/m ²
		mg/dose	doses					
Pediatric	2	5	1	5	12	0.42	25	10.42
Adult	>12	10	1	10	50	0.20	37	7.40

	route	mg/kg/d	conv. factor	mg/m ²	Dose Ratio		Rounded Dose Ratio	
					Adults	Children	Adults	Children
<u>Carcinogenicity:</u>								
rat			6	0	---	---	---	---
mouse			3	0	---	---	---	---
extra			---	---	---	---	---	---
extra			---	---	---	---	---	---
extra			---	---	---	---	---	---
<u>Reproduction and Fertility:</u>								
rat	oral	64	6	384	51.9	N/A	50	N/A
rat	oral	24	6	144	19.5	N/A	20	N/A
dog			20	0	---	N/A	---	N/A
dog			20	0	---	N/A	---	N/A
<u>Teratogenicity:</u>								
mouse			3	0	---	N/A	---	N/A
rat	oral	96	6	576	77.8	N/A	80	N/A
rabbit	oral	96	12	1152	155.7	N/A	160	N/A
rat			6	0	---	N/A	---	N/A
rabbit			12	0	---	N/A	---	N/A
<u>Overdosage:</u>								
mouse	oral	6000	3	15000	2027.0	1440	2000	1400
rat	oral	5000	6	30000	4054.1	2880	4100	2900
dog			20	0	---	---	---	---
rabbit			12	0	---	---	---	---
<u>Other: Overdosage</u>								
rat	oral	125	6	750	101.4	72	100	70
monkey	oral	1280	12	15360	2075.7	1474.56	2100	1500
extra			---	---	---	---	---	---
extra			---	---	---	---	---	---
extra			---	---	---	---	---	---