

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**022578Orig1s000**

**PHARMACOLOGY REVIEW(S)**

**PHARMACOLOGY/TOXICOLOGY MEMO TO FILE**

**NDA number:** 22-578; 505(b)(1) for Zyrtec Orally Disintegrating Tablets

Relevant NDA's:

NDA 19-835/SE6-022 Zyrtec Tablets (5 & 10 mg)

NDA 21-150/SE6-007 Zyrtec-D 12 Hour

NDA 21-621/SE6-005 Zyrtec Chewable Tablets

NDA 22-155 Zyrtec Syrup

**Review number:** 1

**Sequence number/date/type of submission:** SN 000, November 9, 2009

**Information to sponsor:** Yes ( ) No (x)

**Sponsor and/or agent:** McNeil Consumer HealthCare

**Reviewer name:** Wafa A. Harrouk, Ph.D.

**Division name:** Division of Non-Prescription Clinical Evaluation, ODEIV

**HFD #:** 560

**Review completion date:** July 7, 2010

**Drug:**

Generic name: Zyrtec Orally Disintegrating Tablets, 10 mg

Chemical name: Cetirizine HCl (10 mg)

**Drug class:** H<sub>1</sub> receptor antagonist which acts as an antihistaminic agent

**Intended clinical population:** For the temporary relief of symptoms associated with hay fever and other upper respiratory allergies.

**Overview:** The original prescription NDA was approved on December 8, 1995. The proposed OTC product, Zyrtec 10 mg ODT, is targeting a dosing regimen that does not require swallowing a tablet whole and may be dosed with or without water for the relief of allergies but will not include labeling for itching due to hives. The proposed dose will be labeled for a tablet once daily. The results of the bioequivalence trial showed that, under fasted conditions, Zyrtec ODT taken with or without water is bioequivalent to the already approved Zyrtec immediate release tablet taken with water.

**Route of administration:** Oral tablets

**Nonclinical safety issues relevant to clinical use:** None. This 505(b)(1) NDA application for ZYRTEC ODT referenced the original NDA data and the agency's findings of safety and effectiveness of nonclinical data submitted by the same sponsor under NDA # 19-835.

**Overall conclusions and recommendations:** No pharmacology/toxicology safety issues were identified for this NDA. The safety of Cetirizine HCl (10 mg) (Zyrtec tablets) has been established at the time of approval of the Zyrtec prescription tablets. No further non-clinical testing is recommended. This NDA can be approved from the perspective of the pharmacology/toxicology discipline.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22578	ORIG-1	MCNEIL CONSUMER HEALTHCARE DIV MCNEIL PPC INC	CETIRIZINE HCL ORALLY 10MG TABS

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/s/

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WAFI HARROUK  
07/07/2010

PAUL C BROWN  
07/07/2010

## PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR A NEW NDA/BLA

**NDA Number:** 22-578

**Applicant:** McNeil Consumer  
Healthcare

**Stamp Date:** November 9, 2009

**Drug Name:** 10 mg Zyrtec®  
(cetirizine HCl), orally  
disintegrating tablets

**NDA Type:** 505(b)(1)

Background: NDA 22-578 is a new proposed orally disintegrating tablet formulation for ZYRTEC (cetirizine HCl 10 mg) which was submitted as a 505(b)(1) in November 2009. ZYRTEC was initially approved as a prescription drug in 1995 and was later switched for over the counter (OTC) use in 2007 for the temporarily relief of symptoms due to hay fever or other upper respiratory allergies (runny nose, sneezing, itchy, watery eyes, itching of the nose or throat) and for the relief of itching due to hives (urticaria) in adults and children 6 years of age and older (5 mg & 10 mg tablets, 5 mg & 10 mg chewable tablets, and syrup 1 mg/mL dosage forms). The syrup formulation was approved for children aged 2-5 years of age for the temporary relief of symptoms of hay fever or other upper respiratory allergies. The proposed 10 mg ODT is targeting a dosing regimen that does not require swallowing a tablet whole and may be dosed with or without water for the relief of allergies but will not include labeling for itching due to hives. This 505(b)(1) NDA application for ZYRTEC will rely on the agency's previous finding of safety and effectiveness of nonclinical data for ZYRTEC under NDA 19-835 (approved in 1995). =

On **initial** overview of the NDA application: There are no outstanding pharmacology/toxicology issues since the sponsor will be referring to data submitted under the prescription NDA.

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comment</b>
1	On its face, is the pharmacology/toxicology section of the NDA organized (in accord with 21 CFR 314 and current guidelines for format and content) in a manner to allow substantive review to begin?			N/A
2	Is the pharmacology/toxicology section of the NDA indexed and paginated in a manner allowing substantive review to begin?			N/A
3	On its face, is the pharmacology/toxicology section of the NDA legible so that substantive review can begin?			N/A
4	Are all required (*) and requested IND studies (in accord with 505 b1 and b2 including referenced literature) completed and submitted in this NDA (carcinogenicity, mutagenicity*, teratogenicity*, effects on fertility, juvenile studies, acute and repeat	x		

## PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR A NEW NDA/BLA

	Content Parameter	Yes	No	Comment
	dose adult animal studies*, animal ADME studies, safety pharmacology, etc)?			
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, have studies by the appropriate route been conducted with appropriate formulations? (For other than the oral route, some studies may be by routes different from the clinical route intentionally and by desire of the FDA).	x		The sponsor has conducted a bioequivalence pharmacokinetic study to compare the new formulation to a previously approved formulation
6	On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the sponsor <u>submitted</u> a rationale to justify the alternative route?	x		
7	Has the sponsor <u>submitted</u> a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) <u>or</u> an explanation for any significant deviations?			N/A
8	Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?			N/A
9	Are the proposed labeling sections relative to pharmacology/toxicology appropriate (including human dose multiples expressed in either mg/m2 or comparative serum/plasma levels) and in accordance with 201.57?			N/A
10	If there are any impurity – etc. issues, have these been addressed? (New toxicity studies may not be needed.)			N/A
11	Has the sponsor addressed any abuse potential issues in the submission?			N/A
12	If this NDA is to support a Rx to OTC switch, have all relevant studies been submitted?			N/A
13	From a pharmacology/toxicology perspective, is the NDA fileable? If ``no`` please state below why it is not.	x		

Application  
Type/Number

Submission  
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Submitter Name

Product Name

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NDA-22578

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ORIG-1

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MCNEIL  
CONSUMER  
HEALTHCARE DIV  
MCNEIL PPC INC

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CETIRIZINE HCL ORALLY 10MG  
TABS

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/s/  
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WAFI HARROUK  
03/11/2010