U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA #:	21252
Drug Name:	CANASA Suppository (Mesalamine 1000 mg)
Indication(s):	Mild To Moderately Active Ulcerative Proctitis (UP)
Applicant:	Forest Laboratories, LLC
Date(s): Stamp: PDUFA:	 March 11, 2016 September 11, 2016
Review Priority:	Standard
Biometrics Division:	Division of Biometrics 3
Statistical Team: Reviewer: Team Leader:	 Shahla Farr, MS Yeh-Fong Chen, PhD
Medical Division:	Division of Gastroenterology and Inborn Errors Products
Clinical Team: Reviewer: Team Leader: Project Manager:	 Marjorie Dannis, MD Anil Rajpal, MD Kelly Richards,
EDR Location: \\CDSESUB1\evsprod\NDA021252\021252.enx **SharePoint:**	
Keywords: NDA review, clinical study	

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1. EXECUTIVE SUMMARY

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2. BACKGROUND

The CANASA® (mesalamine) 500 mg rectal suppositories New Drug Application (NDA) 21-252, for the treatment of active ulcerative proctitis (UP) in adults, was submitted by Axcan Scandipharm, Inc. (Axcan) and approved by the Food and Drug Administration (FDA) on 5 Jan 2001. The supplemental NDA (sNDA) for the 1000 mg dose was approved on 5 Nov 2004. In accordance with the Pediatric Research Equity Act (PREA), the NDA approval letter included a post-marketing commitment (PMR) 633-2 to conduct a clinical efficacy trial in pediatric patients with ulcerative proctitis, aged 12-18 years.

Axcan submitted the pediatric study protocol ASPD01-CUS01 in February 2002 and a Pediatric sNDA (S-014) on 28 Sep 2010. (b) (4)

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In March 2012, Axcan merged with Eurand and was renamed Aptalis. In February 2014, Forest Laboratories, LLC (Forest) acquired Aptalis and assumed sponsorship of Canasa (mesalamine). (b) (4)

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In a General Advice letter dated 15 Apr 2015, the Agency recommended that the **PK component of the efficacy study should still be conducted**.

The Sponsor requested a Type C meeting with the Agency to clarify the discussion of the pediatric PMR 633-2 and whether the full PK profile of mesalamine after rectal suppository administration is still necessary. The meeting was granted and took place on 18 Nov 2015. During this meeting, the

(b) (4)

Furthermore, the source data used in the estimation of pediatric exposure following Canasa administration, as well as market-use data was also requested. It was agreed with the Agency that an additional PK study is likely not feasible. It was also agreed that the requested information would be provided (b) (4) for the pediatric sNDA 21-252/S-014 in order to fulfill PMR 633-2.

As requested by the Agency, Forest was to analyze the data from the subset of pediatric patients who had histologically-confirmed UP in Study ASPD01-CUS01.

The purpose of this Type C Pediatric Post Marketing Requirement meeting would be to discuss the (b) (4) pediatric study under PREA for the treatment of active ulcerative proctitis in pediatric patients age 5 to 17 years. (b) (4)

In an information request (IR) dated October 14, 2010, the FDA asked the sponsor to perform a descriptive analysis comparing the efficacy data observed in the pediatric study to the results from adult Canasa® studies.

The clinical study report for the pediatric Study ASPD01-CUS01 and the clinical and safety summaries were previously submitted on 28 Sep 2010 in the original Pediatric sNDA 21-252/S-014 (eCTD Sequence 0000). (b) (4)

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3. STUDY DESIGN AND RESULTS

Study ASPD01-CUS01 was a multicenter, open label, parallel group study and was designed to assess the efficacy and safety of mesalamine 500 mg suppository, taken once daily in the evening (HS), or twice daily (BID) for a 6-week treatment period in relapsing pediatric patients (aged 6-17 years) diagnosed with active UP. The primary efficacy parameter for this study was the DAI score change from Baseline to Week 6 using a last observation carried forward (LOCF) approach.

A total of 49 subjects were enrolled across 15 sites located in the United States, Canada 4 sites) and Poland. Only 14 patients fulfilled all inclusion criteria by also having histologically-confirmed UP.

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/s/

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07/08/2016

YEH FONG CHEN
07/11/2016