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APPLICATION NUMBER:

210867Orig1s000

NON-CLINICAL REVIEW(S)

Tertiary Pharmacology/Toxicology Review

From: Timothy J. McGovern, Ph.D., ODE Associate Director for Pharmacology and Toxicology, OND IO
NDA: 210867
Agency receipt date: October 13, 2017
Drug: Moxidectin
Sponsor: Medicines Development for Global Health

Indication: Treatment of onchocerciasis

Reviewing Division: Division of Antiviral Products

The pharmacology/toxicology reviewer and supervisor concluded that the nonclinical data support approval of ibalizumab for the indication listed above.

Moxidectin is a semisynthetic derivative of a fermentation product of *Streptomyces cyanogriseus*. It is a broad spectrum endectocide that inhibits the development of embryos and sperm in adult filarial worms. The drug is a first-in-class new molecular entity and was granted both orphan drug status and breakthrough therapy designation. It is proposed to be administered as a single oral dose of 8 mg. The plasma half-life in patients (approximately 24 days) is longer than in rats (18-30 hours) and dogs (8-20 days).

The nonclinical program primarily consists of repeat-dose toxicity studies in rats (up to 3 months) and dogs (up to one year). The only general toxicities identified were transient CNS-related clinical signs and anorexia.

Moxidectin was negative in a battery of genotoxicity studies. A carcinogenicity assessment in rats and mice was conducted. While initial results appear to be negative, a comprehensive review requires submission of an electronic dataset for statistical evaluation. (b) (4)

Moxidectin was not associated with fertility or embryo-fetal developmental effects. However, a pre/postnatal development study identified reduced survival and body weight of first generation offspring during the lactation period at a dose slightly above the recommended clinical dose and reduced number of live fetuses at birth at a dose approximating 13 times the human dose. Since the study did not evaluate physical development and neurological function, a new pre/postnatal development study will be conducted as a post-marketing requirement.

Conclusion:
I agree with the Division pharmacology/toxicology conclusion that moxidectin can be approved from the nonclinical perspective. I have reviewed the proposed wording for the nonclinical sections of the product label and agree with the Division recommendations.

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/s/

TIMOTHY J MCGOVERN
06/08/2018

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY NDA/BLA REVIEW AND EVALUATION

Application number:	210867
Supporting document/s:	SD #001
Applicant's letter date:	10/13/2017
CDER stamp date:	10/13/2017
Product:	Moxidectin
Indication:	Treatment of Onchocerciasis (River Blindness)
Applicant:	Medicines Development for Global Health (MDGH)
Review Division:	Division of Anti-infective Products
Reviewer:	James S. Wild, Ph.D.
Supervisor/Team Leader:	Terry Miller, Ph.D.
Division Director:	Sumathi Nambiar, M.D., M.P.H.
Project Manager:	Kristine Parks, Ph.D.

Template Version: September 1, 2010

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TABLE OF CONTENTS

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