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APPLICATION NUMBER:

22483Orig1s000

CROSS DISCIPLINE TEAM LEADER REVIEW

Cross-Discipline Team Leader Addendum

Date	3.12.2010
From	Jill Lindstrom, MD
Subject	Cross-Discipline Team Leader Review
NDA #	22-483
Applicant	Graceway Pharmaceuticals, LLC
Date of Class 1 Re-Submission	1.29.2010
PDUFA Goal Date	3.29.2010
Medical Officer	Milena Lolic, MD
Project Manager	Kelisha Turner
Proprietary Name / Established (USAN) names	ZYCLARA/imiquimod
Dosage forms / Strength	Cream/3.75%
Proposed Indication(s)	Topical treatment of clinically typical, non-hyperkeratotic, non-hypertrophic actinic keratoses (AK) on the face or scalp in immunocompetent adults
Recommended:	<i>Approval</i>

This Addendum to my review dated 9.23.2009 of the original submission for NDA 22-483 will address the issue articulated in the Complete Response Action letter dated 10.16.2009. The reader is also referred to the review of the resubmission by Dr. Milena Lolic and the Dispute Appeal Response letter dated 1.15.2010.

The Complete Response Action letter listed the following information need:

Conduct of a thorough QT study with Holter monitoring to demonstrate the impact of your product on cardiac repolarization and heart rate.

In their resubmission, the applicant provided ECG data which was obtained during the development of Aldara (imiquimod) 5% cream but not included with the original submission or provided during the first review cycle of NDA 22-483.

Consultative review was obtained from the QT Interdisciplinary Review Team regarding the adequacy of this data to address the impact of imiquimod on QT interval. The QT-IRT found the submitted data, “are sufficient,” and that “further study is [not] needed to characterize imiquimod’s effect on QT.”

I concur with the recommendation of Dr. Lolic and the multidisciplinary review team that the application be approved, pending agreement on labeling (under review at the time of close of this addendum), with the following postmarketing requirement:

Conduct 2-way cross-over trial in at least 100 subjects with actinic keratoses on the face to assess the effect of topical imiquimod on the cardiac rhythm. Zyclara 3.75% cream should be used as labeled, and event-monitoring (via external event recorder with loop recording capability) should be performed during all of the treatment phases (first and second 2-week treatment periods for both test articles).

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22483	ORIG-1	GRACEWAY PHARMACEUTICA LS LLC	IMIQUIMOD 3.75% CREAM

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/s/

JILL A LINDSTROM
03/12/2010