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APPLICATION NUMBER:

21-729

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

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Clinical Pharmacology and Biopharmaceutics Comment

NDA:	21-729
Drug:	Aripiprazole Orally Disintegrating Tablet
Trade Name:	Abilify ODT Discmelt
Strengths:	[redacted] 10 mg, 15 mg, 20mg, 30 mg Oral Disintegrating Tablets
Applicant:	Bristol Myers Squibb
Indication:	Treatment of Schizophrenia
Submission Type:	Response to Approvable Letter
Submission Date:	12/12/05
OND Division:	DPP (HFD-130)
OCPB Division:	DCPB1 (HFD-860)
Reviewer:	Kofi A. Kumi, Ph.D.
Team Leader:	Raman Baweja, Ph.D.

Background

The sponsor submitted NDA 21-729 for Abilify Discmelt Orally Disintegrating Tablets on December 22, 2003. An Approvable letter was issued on October 22, 2004. In this correspondence, the sponsor has submitted complete response to questions/comments that were included in the Approvable letter. This comment is related to Question No. 10, which was provided by OCPB to be included in the Approvable letter.

Question: We request that you adopt the following dissolution method and specification

Apparatus:	USP Apparatus II (Paddle)
Speed:	75 rpm
Media:	pH 4 Acetate Buffer
Volume:	1000 mL

Specification: Q NLT [redacted] in 30 minutes

The sponsor has agreed to adopt the method but would like to adopt an interim dissolution specification of Q NLT [redacted] in 30 minutes instead of a specification Q NLT [redacted] in 30 minutes.

The sponsor's rationale for an interim specification is that the proposed specification has no clinical relevance because the dissolution specification for the tablet was Q NLT [redacted]. However, the proposed method for the ODT and that for the tablet are different. The dissolution method for the tablet is

Apparatus:	USP Apparatus II (Paddle)
Speed:	60 rpm
Media:	pH 1.2 USP Buffer
Volume:	1000 mL

The Abilify tablet method was not chosen as the dissolution method for Abilify Discmelt ODT due to rapid dissolution, high variability, and loss of discriminatory ability for detecting changes in the ODT. Also, the sponsor indicates that a Q NLT [redacted] would increase [redacted] requirement as compared to the frequency of [redacted] that would occur under the dissolution specification of Q NLT [redacted] in 30 minutes. The sponsor argues that a dissolution specification tighter than NLT [redacted], in 30 minutes would not provide additional indication of product performance. Hence, the

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sponsor is proposing an interim dissolution specification of Q NLT [redacted] in 30 minutes. A final dissolution specification would to be set for aripiprazole ODT once the sponsor gains experience in full-scale manufacturing of at least [redacted] batches.

Comment to Sponsor:

1. The sponsor's proposal for an interim specification of Q NLT [redacted] in 30 minutes is acceptable. However, the sponsor should provide full dissolution profiles for at least [redacted] batches or batches produced for 12 months, whichever comes first, and should also provide data indicating how many [redacted] would be performed if the specification is set at Q NLT [redacted] A final specification would be set after the data is provided and reviewed.
2. The sponsor should provide the data requested in #1 above within 16 months of the date of the action letter
3. Please forward comments 1 and 2 to sponsor.

Kofi A. Kumi, Ph.D._____

RD/FT Initialed by Raman Baweja, Ph.D._____

CC:NDA 21-729, HFD-130, HFD-860 (Mehta, Baweja, KumiK), EDR (Biopharm)

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/s/

Kofi Kumi
2/22/2006 12:25:30 PM
BIOPHARMACEUTICS

Raman Baweja
2/22/2006 06:29:56 PM
BIOPHARMACEUTICS

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Clinical Pharmacology and Biopharmaceutics Review

NDA: 21-729
Drug: Aripiprazole
Trade: Abilify™ ODT
Strengths: [redacted] 10 mg, 15 mg, 20mg, 30 mg Oral Disintegrating Tablets
Applicant: Bristol Myers Squibb
Indication: Treatment of Schizophrenia
Submission Type: New Formulation
Related IND and NDA: IND 62, 181 and NDA 21-436
Submission Dates: 12/22/03, 3/31/04, 7/8/04, 8/4/04
OND Division: DNDP (HFD-120)
OCPB Division: DPE1 (HFD-860)
Reviewer: Kofi A. Kumi, Ph.D.
Team Leader (Acting): Sally Yasuda, Pharm.D.

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