CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-729

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 21-729 SUPPL # 000 HFD # 130

Trade Name Abilify Discmelt 10, 15, 20, 30mg

Generic Name aripiprazole orally disintegrating tablets

Applicant Name Otsuka Pharmaceutical Co., Ltd.

Approval Date, If Known June 7, 2006

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☐ NO ☒

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

N/A

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☐ NO ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☒ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21-713 Abilify Oral Solution

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☒

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☐ NO ☒

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☐ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☐

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☐

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☐

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		!
		!
IND #	YES ☐	! NO ☐
		! Explain:
Investigation #2		!
		!
IND #	YES ☐	! NO ☐
		! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☐

If yes, explain:

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Name of person completing form: Keith Kiedrow, PharmD, LT USPHS
Title: Regulatory Project Manager
Date: 6/7/2006

Name of Office/Division Director signing form: Thomas Laughren, MD
Title: Director, Division of Psychiatry Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Laughren
6/11/2006 11:07:04 AM

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO 22, MAIL STOP 4447)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**OSE CONSULT #:**
May 4, 2006	May 29, 2006	04-0091-1, 05-0198
DATE OF DOCUMENT:	**PDUFA DATE:**	
December 12, 2005	June 13, 2006	

TO: Thomas Laughren, MD
Director, Division of Psychiatry Products
HFD-130

THROUGH: Alina Mahmud, R.Ph., M.S., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support

FROM: Kimberly Pedersen, R.Ph., Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME:	**SPONSOR:** Otsuka America Pharmaceutical, Inc.
Abilify® Discmelt™ (Aripiprazole Orally Disintegrating Tablets) 10 mg, 15 mg, 20 mg and 30 mg **NDA#:** 21-729	

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Abilify® Discmelt™. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections base upon approval of other proprietary or established names from the signature date of this document.

2. Subsequent to a review of the post-marketing reports associated with the currently marketed Abilify drug product, DMETS recommends implementation of the label revisions outlined in Section III to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name Abilify® Discmelt™ acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, Project Manager, at 301-796-0538.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
WO 22, MAIL STOP 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 16, 2006

NDA #: 21-729

NAME OF DRUG: **Abilify® Discmelt™**
(Aripiprazole Orally Disintegrating Tablets)
10 mg, 15 mg, 20 mg and 30 mg

NDA SPONSOR: **Otsuka America Pharmaceutical, Inc.**

NOTE: This review contains proprietary and confidential information that should not be released to the public.

I. INTRODUCTION

This consult was written in response to a request from the Division of Psychiatry Products (HFD-130), for an assessment of the proprietary name Abilify® Discmelt™ in regard to the potential name confusion with other proprietary or established drug names. Container labels (blister foils) and carton labeling were provided for review and comment.

PRODUCT INFORMATION

Abilify® Discmelt™ is a psychotropic medication indicated for the treatment of schizophrenia. Abilify® Discmelt™ is an orally disintegrating tablet available in 10 mg, 15 mg, 20 mg and 30 mg strengths, which will available in package sizes of thirty and one-hundred tablets. The recommended starting dose for schizophrenia is 10 or 15 mg daily without regard to meals. The recommended starting dose for bipolar disorder is 30 mg once daily.

Patients should open the blister when ready to administer. In order to open the blister package, the patient should peel back the foil to expose the tablet. Attempts to push the tablet through the foil could result in damage. Immediately after opening the package, the patient should remove the tablet with dry hands and place the tablet on the tongue. The tablet should disintegrate rapidly. The sponsor recommends the discmelt be taken without liquid; however, it can be used if needed. The patient should not attempt to split the tablet.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[i,ii] as well as several FDA databases[iii,iv] for existing drug names which sound-alike or look-alike to Abilify® Discmelt™ to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[v]. The SAEGIS[vi] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Abilify® Discmelt™. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff with representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name Abilify® Discmelt™ acceptable from a promotional perspective.

2. The Expert Panel identified the currently marketed Abilify tablets and Abilify oral solution as to having the potential for confusion with Abilify® Discmelt™. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Look-Alike Names Identified for Elaprase

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other**
Abilify® Discmelt™	Aripiprazole Orally Disintegrating Tablets 10mg, 15 mg, 20 mg, 30 mg	10 mg to 30 mg daily	
Abilify	Aripiprazole Tablets: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg Oral Solution: 1 mg/mL, 150 mL bottle	10 mg to 30 mg daily	LA/SA
*Frequently used, not all-inclusive. **LA (look-alike)/SA (sound-alike).			

[i] MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

[ii] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.

[iii] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

[iv] Phonetic and Orthographic Computer Analysis (POCA)

[v] www location http://www.uspto.gov/tmdb/index.html.

[vi] Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

B. SAFETY EVALUATOR RISK ASSESSMENT

1. AERS and DQRS Searches

As there are two dosage forms of Abilify currently marketed (tablets and oral solution), DMETS determined the best method to ascertain if the potential for name confusion exists is to review the post-marketing safety reports in the FDA databases. DMETS conducted searches of the FDA Adverse Event Reporting System (AERS) and the Drug Quality Reporting System (DQRS) to determine the degree of post-marketing errors with Abilify. AERS was searched using the following MedDRA terminology and drug names: Preferred Term (PT) "Pharmaceutical Product Complaint" and High Level Group Term (HLGT) "Medication Errors" with "Abili%" and Aripi%" for drug names. This search strategy uncovered one-hundred eighty three reports (n=183). The majority of these reports involved adverse events (including potential drug interactions), exposure in pregnancy, overdoses, and a number of duplicate reports. To further clarify, the overdose reports were related to and unrelated to the drug product of Abilify and included intentional and unintentional overdoses (including extra doses received and child exposures). These reports appear to relate to the indication of the drug product (i.e. multiple drug therapies, expected adverse events such as suicidal tendencies, etc); thus, DMETS will not discuss these errors further as they do not relate to the proprietary name, labels or labeling. Thirteen cases did, however, relate to the proprietary name, labels and labeling. These cases will be discussed further below.

a. Established Name Confusion (n=4)

The established name of Abilify is Aripiprazole which contains the USAN stem for proton pump inhibitors (–prazole). However, Abilify or Aripiprazole is not a proton pump inhibitor. Thus it came as no surprise that there were four cases of confusion with the established name. One case was received in 2002 (the year of Abilify approval, November 2002) with the remaining three dated early 2003. Two cases noted formulary substitutions with lansoprazole, which were caught prior to administration and the remaining two reporters addressed concerns with the name similarities. As these cases were received early in the approval of Abilify with no subsequent complaints, DMETS suspects practitioners have become familiar with the drug product's established name and thus, no action is required at this time.

b. Wrong Drug Product (n=2)

Two cases described confusion with other marketed drug products. The first case (2006) described an error in which a prescription was filled with Abilify in lieu of Actos. This case was poorly documented, but DMETS notes that the drug products share similar strengths (15 mg and 30 mg), dosing frequency (daily), and dosage form (tablet). In addition, the products could share similar placement on the pharmacy shelves. However, the color schemes for the bottle trade dress are different (Actos in green/white and blue/white compared to the peach/yellow and blue of Abilify). The second case described a cognitive error by a nurse who called in a prescription for Zyprexa 2.5 mg BID, when Abilify 2.5 mg BID was intended. These drug products share indication (schizophrenia and bipolar disorder), strength (2.5 mg, 5 mg, 10 mg, 15 mg and 20 mg), dosing frequency (daily), and dosage form (tablets). As there is only one case for each drug product, DMETS does not recommend regulatory action at this time, but will continue to monitor for any further confusion.

c. Wrong Strength (n=7)

Seven medication error cases, all occurring at the pharmacy level, implicate confusion between the strengths of Abilify. Four of the seven cases implicate selection error as the error involved a refill (n=3) or the correct label but wrong drug (n=1). There is no consistency based on the strength ordered and the incorrect strength dispensed (see table 2).

Table 2

AERS # (Year)	Patient Age (years)	New or Refill	Ordered	Dispensed	Outcome (note)
4212338-1 (2002)	10	New	5 mg	15 mg	Lethargy, difficult to arouse, gasping, dilated pupils 2nd occurrence in retail pharmacy setting
4187681-5 (2003)	13	Refill	15 mg	10 mg	Chest pain and tachycardia
4305627-3 (2003)	34	New	5 mg	15 mg	Vomiting
4370282-3 (2004)	9	New	5 mg	30 mg	"out of control"
4592412-0 (2005)	6	Unk	5 mg	30 mg	No adverse effects at the time of reporting
4675409-1 (2005)	12	Refill	5 mg	30 mg	Drowsy, "upset stomach", emergency room visit with unspecified treatment
4675497-2 (2005)	Unk	Unk	5 mg	10 mg	None indicated (poorly documented case)
4755617-1 (2005)	Unk	New	5 mg	10 mg	Somnolence (poorly documented case)

DMETS would like to acknowledge that the majority of these cases involve children (n=5). However, the product labeling denotes that the safety and effectiveness of Abilify in the pediatric and adolescent populations has not been established. The majority of the cases resulted in a negative outcome, but none appeared to result in hospitalization or other "severe" outcomes. It is difficult to ascertain causality from the cases based on the information provided.

Upon review of the labels and labeling, DMETS notes that the strengths are differentiated with different colors that correspond to the color of the tablet. DMETS believes that this helps patients and practitioners identify the strength of Abilify once it is dispensed. DMETS notes that the labels/labeling and the tablet color of the 10 mg and 30 mg strengths have similar coloring schemes. However, no medication errors have been reported between the 10 mg and 30 mg strengths. The ordered strength in six of the seven cases was 5 mg, however 10 mg, 15 mg, and 30 mg strengths were dispensed in error. There is no similarity in color between the 5 mg tablets and these other strengths. However, the sponsor's trade dress utilizes colors that dominate the labels and distracts attention away from the presentation of the product strength. Other factors that could have contributed to these errors include increased Abilify prescription writing, busy pharmacies (lack of appropriate attention to detail), computer selection error (of the correct strength), or proximity on the shelf (literal mispull from the shelf). DMETS recommends that the labels and labeling for the proposed Abilify Discmelt be completely different than those currently marketed for Abilify tablets. Additionally, to address the current confusion within the Abilify Tablet product line we recommend increasing the presentation of the strength so that it is more prominently displayed.

2. Abilify® Discmelt™ Name Review

Abilify Discmelt is the latest product extension to Abilify. Abilify is currently approved as a tablet and oral solution dosage form. Since the currently marketed Abilify and proposed Abilify Discmelt share the same root name, there is concern that confusion may occur if the "Discmelt" modifier is omitted, overlooked, or disregarded. Since the search of the FDA databases found confusion between the different strengths of the currently marketed Abilify tablets, DMETS has reason to suspect that this may occur within the proposed orally disintegrating tablet strengths and between this proposed tablet and the currently marketed tablet. Both products share the same product characteristics (i.e. strength, dosing frequency, etc). However, the package insert details that the products are bioequivalent. Thus if the patient were to receive the incorrect dosage form, there would be no resultant harm. However, DMETS is concerned if the bioequivalency would be identical if the drug product were incorrectly administered. If the prescription was written for the disintegrating tablet and the oral tablet dispensed, would the patient experience any adverse effects from chewing the tablet? Conversely, would the efficacy be comparable if the disintegrating tablet were swallowed? The package insert reads that the disintegrating tablet is preferred to be administered without water, but what occurs when administered with water (as in usual tablet ingestion)? DMETS has contacted the review Division for answers to these questions.

DMETS suspects dispensing errors will be inevitable when the proposed product is initially marketed. However suggestions to help minimize confusion such as differentiating trade dress and establishing educational campaigns/marketing plans are included in detail in Section III.

3. The modifier Discmelt™

A search of the standard pharmaceutical databases and proposed names in DMETS found many drug products available in orally disintegrating tablet dosage forms with and without modifiers to discern this different dosage form. DMETS notes that there is no universal modifier for indicating a product as an orally disintegrating tablet. Additionally, since the term "discmelt" sounds like a dosage form and not a novel drug product name such as Zydis, we believe the possibility for drug identification confusion is limited. When the term "Zydis" was first introduced, healthcare practitioners thought Zydis meant a different product rather than an orally disintegrating tablet. There will likely be confusion when Abilify Discmelt is first marketed, practitioners may not be aware of the existence of the orally disintegrating tablet. Thus, DMETS recommends the sponsor educate patients and practitioners on the availability of this dosage form and its respective modifier.

C. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

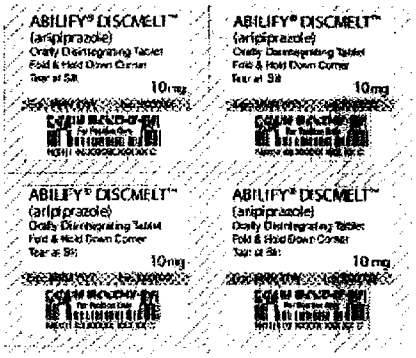
In review of the Abilify® Discmelt™ container label (blister foils) and carton labeling, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

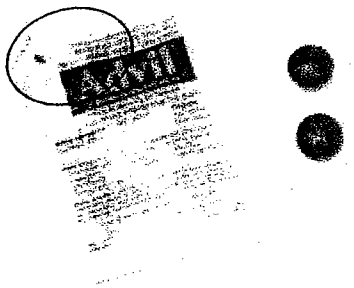
1. GENERAL COMMENTS

   As this is the introduction of another dosage form to a currently marketed product line with existing and continued errors in dosing and administration, DMETS recommends the sponsor educate patients and health care practitioners on the availability of the new dosage form and the proper use of this product.

2. CONTAINER LABEL (Individual Blisters)

   a. As currently presented (see below on left), the directions to open the package are not clear ("Fold and Hold Down Corner, Tear at Slit"). As the orally disintegrating tablets are fragile, errors in opening could result in tablet damage. DMETS recommends the sponsor better describe how to open the foil blister by further descriptive terms or by indication (by dotted line, see Advil example below) specifically where to open the package.





   b. To assure the tablets maintain their integrity, DMETS recommends the sponsor add a statement to warn the patient that attempting to push the tablet through the foil could result in damage to the tablet. This could be printed on the front or back of the foil blister.

   c. In order to better recognize the blister contents, DMETS recommends the strength be relocated adjacent to or immediately following the established name and given greater prominence. There should be no intervening matter between the name and the strength. As currently presented, DMETS fears the strength may be lost in the color pattern and lot/expiration information.

   d. Adjust the font size and font style of the established name (both aripiprazole and orally disintegrating tablet) so that they are uniform.

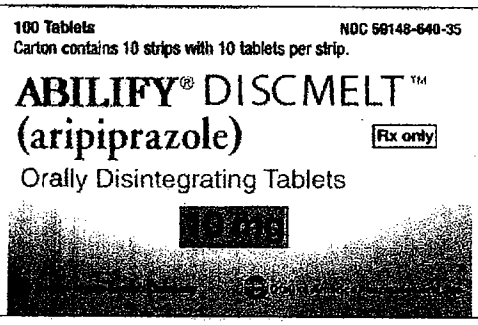
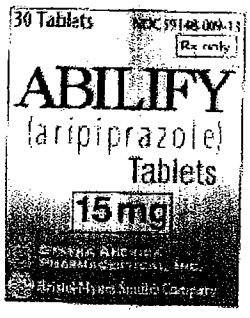
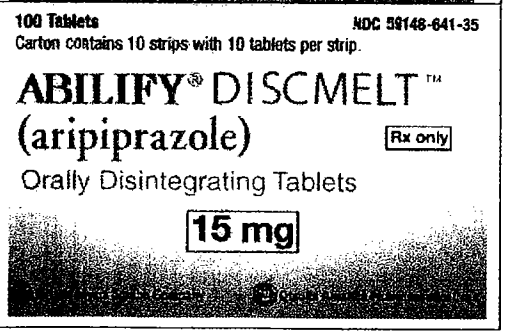
3. CARTON LABELING

a. As reports from the FDA databases indicate confusion between strengths of the currently marketed Abilify tablets, we can anticipate similar confusion with the Discmelt product as well as confusion between the Discmelt and oral tablets. Thus, it is imperative to distinguish between the proposed "discmelt" and the currently marketed tablets. DMETS notes that the color scheme (blue and yellow) for the Abilify product line is identical (see Table 3). This color scheme dominates the labels and labeling which distracts attention away from the presentation of strength. Furthermore, DMETS notes that the colors used for the matching strengths of the orally disintegrating tablets and currently marketed tablets are identical with the exception of the speckles (see Table 3). Therefore, in order to minimize medication errors we recommend the following:

i. DMETS recommends that a different trade dress and color scheme be utilized for the proposed orally disintegrated tablets. This color scheme should not dominate the labels and labeling. As currently presented, the established name and strength are lost in the stylized background. Information, such as the proprietary name, established name and strength should be the most prominent information presented on the principal display panel. Revise to eliminate these colors or mute them.

ii. The corresponding color of the strengths on the carton labeling are the same for both the Abilify and Abilify Discmelt tablets. DMETS does not recommend using the same colors for both products. DMETS recommends that the colors used for the presentation of the strength either be identical to the actual color of the tablets (e.g., yellow with scattered specks for the 15 mg orally disintegrating tablet) or use entirely different colors where none of the strengths overlap the currently marketed Abilify Tablets. Regardless of the method used the color of the Abilify Tablet strengths and Abilify Discmelt strengths should be clearly differentiated from each other.

Table 3:

	Tablets	**Discmelt**
Abilify 10 mg		
Abilify 15 mg		

b. The presentation of the established name should be in the same font style and size as the dosage form. As currently presented, the "Orally disintegrating Tablets" does not have prominence which may result in a lack of name recognition leading to medication error.

c. In order to accommodate for the changes to the established name, the "Rx only" statement can be relocated to the lower third of the principal display panel.

d. Revise the net quantity "100 Tablets Carton contains 10 strips with 10 tablets per strip" to read "100 tablets (10 X 10)" in order to reduce the amount of clutter on the principal display panel.

4. INSERT LABELING

a. Dosage and Administration

i. Under "Directions for Use of Abilify Discmelt...", DMETS questions what occurs if the tablet is taken with water? If there is adverse effect or change in bioavailability? If so, please indicate in this section.

ii. DMETS questions if the orally disintegrating tablets may be taken if they are damaged? Can the orally disintegrating tablet be chewed? Please indicate the answers in the labeling. If the orally disintegrating tablets can not be chewed, this information should also be placed on the container label and carton labeling, if space permits.

b. Storage

Please indicate if the storage for the tablets and orally disintegrating tablets are the same. Currently, the labeling just lists "tablets."

5. CONTAINER LABEL AND CARTON LABELING RECOMMENDATIONS FOR ABILIFY TABLETS (NDA 21-436)

Due to post-marketing errors between the different strengths of the currently marketed Abilify tablets and potential errors with the Discmelt product once approved, DMETS recommends that the labels and labeling of Abilify Tablets and Abilify Discmelt be clearly differentiated by the use of different colors or corporate trade dress. We also recommend increasing the prominence of the strength and utilizing a trade dress that does not dominate the labels and labeling which takes attention away from the presentation of strength.

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/s/

Denise Toyer
5/31/2006 04:29:07 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
5/31/2006 04:37:37 PM
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