CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-925

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; WO22 M/S 4447)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**ODS CONSULT #:** 04-0273-1
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December 7, 2005	April 29, 2006	

TO: Mary Parks, M.D.
Acting Director, Division of Metabolism and Endocrinology Products
HFD-510

THROUGH: Alina R. Mahmud, RPh, MS, Team Leader
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FROM: Tina M. Tezky, Pharm.D., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME:	**IND SPONSOR:** Takeda Pharmaceuticals
Duetact (Pioglitazone HCl and Glimeperide) Tablets [redacted], 30 mg/4 mg, and 30 mg/2 mg **NDA#:** 21-925	

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Duetact. 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 based upon approval of other proprietary or established names from the signature date of this document.

2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name, Duetact, 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 301-827-3242.

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; WO22, M/S 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 6, 2006

NDA#: 21-925

NAME OF DRUG: Duetact™ (Pioglitazone HCl and Glimepiride) Tablets
[redacted], 30 mg/4 mg, and 30 mg/2 mg

NDA HOLDER: Takeda Pharmaceuticals

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 Metabolism and Endocrinology Products (HFD-510) for a review of the proprietary name, "Duetact", regarding potential name confusion with other proprietary and/or established drug names. Container labels, carton, and insert labeling were provided for review and comment.

Pioglitazone HCl and Glimepiride (IND 69,686), was previously reviewed with the trade names [redacted] and [redacted]. In the original review dated November 16, 2004, (ODS Consult #04-0273), the trade names [redacted]

PRODUCT INFORMATION
Duetact is a combination product containing pioglitazone HCl and glimepiride indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus who are already treated with a combination of Actos and a sulfonylurea or whose diabetes is not adequately controlled with a sulfonylurea alone. The usual dosage range is one tablet daily. Duetact will be available in [redacted], 30 mg/4 mg, and 30 mg/2 mg tablets.

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3] for existing drug names which sound-alike or look-alike to Duetact 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[4]. The SAEGIS™ Online service [5] 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. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Duetact. 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 and 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 did not have concerns with the name, Duetact, in regard to promotional claims.

2. The expert panel identified five proprietary names that were thought to have the potential for confusion with Duetact. These products are listed in Table 1 (see page 4), along with the available dosage forms and usual dosage.

[1] 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.

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

[3] 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.

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

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

Table 1: Potential Sound-Alike/Look-Alike Names Identified for Duetact

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Duetact	Pioglitazone/Glimepiride Tablets [redacted] 30 mg/4 mg, 30 mg/2 mg	One tablet once daily.	
Duet Rx	Tablets Chewables Vitamin C 600 mg/Vitamin E 45 IU/Thiamine 15 mg/Riboflavin 10.2 mg/Niacinamide 100 mg/Vitamin B6 10 mg/Vitamin B12 6mcg/Folic Acid 400 mcg/Biotin 300 mcg/Pantothenic Acid 25 mg/Zinc 22.5 mg	One tablet once daily.	LA/SA
Duac Rx	Clindamycin/Benzoyl Peroxide Topical Gel 1%/5%	Apply to affected areas once daily.	SA
AcuTect Rx	Technetium TC-99M Apcitide Injection	Used to diagnose acute venous thrombosis.	LA
Neo Tect Kit Rx	Technetium TC-99M Depreotide Injection	Used to identify cells that may be associated with lung cancer.	LA
Diastat CIV	Diazepam Rectal Gel 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg	0.2 – 0.5 mg/kg, depending on age. Not to be use to treat more than five episodes per month and no more than one episode every five days.	SA

*Frequently used, not all-inclusive.
**LA (look-alike), SA (sound-alike)
***Name pending approval. Not FOI releasable.

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

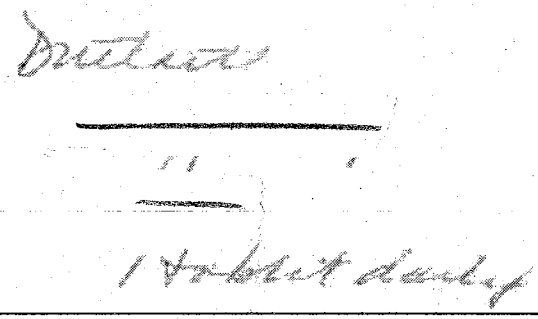
As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Duetact were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Duetact with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 122 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Duetact (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on

voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 	Duetact Dispense Use one tablet daily.
Inpatient RX: 	

2. Results:

   None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Duetact, the primary concerns related to look-alike and sound-alike confusion are with Duet, Duac, AcuTect, Neo Tect Kit, and Diastat. Upon further review of the names gathered from EPD, the names AcuTect and Neo Tect Kit were not reviewed further due to a lack of convincing look-alike/sound-alike similarity with Duetact in addition to numerous differentiating product characteristics including product strength, dosage formulation, indication for use, and frequency of administration.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Duetact.

1. Duet was identified as having look-alike and sound-alike potential with Duetact. Duet is a prenatal multivitamin with minerals and is dosed one tablet daily. The look-alike and sound-alike similarities stem from the fact that name Duet comprises the first four letters of Duetact (DUET vs. DUETACT). The two products share the same dosage form (tablet), route of administration (oral), and frequency of administration (once daily). However, the suffix "-ACT" in Duetact gives the name additional length, providing both phonologic and orthographic differentiation between Duet and Duetact. Since Duetact is available in three different strengths, an indication of strength would be required prior to dispensing. The two medications also differ with respect to the indication for use (vitamin and mineral supplementation vs. Type 2 Diabetes). DMETS believes the differing lengths of the names and presentation of strength will decrease the likelihood for confusion between Duet and Duetact.

Duet
Duetact

2. Duac and Duetact were found to have sound-alike similarities. Duac (clindamycin and benzoyl peroxide) is topical gel indicated for the treatment of inflammatory acne vulgaris. Duac is a combination of clindamycin 1% and benzoyl peroxide 5% and is available as a topical gel in 45 gram tubes. The typical dose is to apply to the affected areas of skin once daily, in the evening. Duac and Duetact contain the same number of syllables (two) which contributes to their sound-alike similarity. The first syllable of each name sounds identical (DU- vs. DUE-); however, the "T" in the middle and at the end of Duetact provides a phonetic differentiation between the two names. Additionally, the two products have differing product characteristics, such as dosage form (topical gel vs. tablet), route of administration (topical vs. oral), dosage strength (1%/5% vs. ———, 30 mg/4 mg, 30 mg/2 mg), and storage conditions (refrigerate vs. room temperature). Due to the product and phonetic differences, DMETS believes the potential for name confusion between Duac and Duetact is minimal.

Duetact
Duac

3. Diastat and Duetact may look-alike depending on how they are scripted. Diastat is a gel formulation of diazepam intended for rectal administration in the management of selected, refractory, patients with epilepsy, on stable regimens of antiepileptic drugs, who require intermittent use of diazepam to control bouts of increased seizure activity. Diastat is a schedule IV controlled substance (CIV) available in a concentration of 5 mg/mL and is provided in 2.5 mg, 5 mg, 10 mg, 15 mg, and 20 mg prefilled, unit-dose, rectal delivery systems. The recommended dose of Diastat is 0.2 – 0.5 mg/kg depending on the age of the patient, rounded upward to the nearest available dose. Diastat is not to be use to treat more than five epileptic episodes per month and no more than one episode every five days. Both names begin with a "D" and end with a "T". The names also have two overlapping middle letters in similar positions (DUETACT vs. DIASTAT), which contributes to their look-alike similarities.

However, different product characteristics such as dosage form (rectal gel vs. tablet), route of administration (rectal vs. oral), frequency of administration (as needed vs. once daily), available strengths (2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg vs. [redacted] 30 mg/4 mg, 30 mg/2 mg) and prescription status (CIV vs. non-scheduled) help distinguish between the two products. To further distinguish the products, Diastat is supplied in pre-filled, unit dose rectal delivery systems and is packaged in a twin pack containing two rectal delivery systems, two packets of lubricating jelly, and patient/caregiver package insert. DMETS believes the product differences will help to avert name confusions between Diastat and Duetact.

Diastat
Duetact

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container labels as well as the carton and insert labeling proposed for Duetact Tablets, DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. The word "duet" in Duetact appears italicized. Emphasis on this portion of the proprietary name will increase the potential for confusion with the currently marketed U.S. product Duet (see section II.D.1 of this review). Revise the font of "duet" so it is consistent with the remainder of the proprietary name in accordance with 21 CFR 201.10(g)(2).

2. We note the sponsor proposes a professional sample size of 30 tablets. DMETS believes this number is inappropriate for a physician sample. Thirty tablets represent a unit-of-use package size appropriate for a one month supply of medication. If allowed, then this package size needs to have child resistant closures to be in compliance with the Poison Prevention Act.

3. The background colors utilized for the container labels of the 30 mg/2 mg and 30 mg/4 mg strengths is purple and light purple, respectively. Although the shades are different, the same color family for both strengths makes it difficult to differentiate between the strengths. We recommend making the packaging more distinct between the two strengths in order to minimize confusion and selection errors between the two product strengths.

B. CONTAINER LABELS (30 COUNT and 90 COUNT BOTTLES)

1. See General Comments A.1 and A.3.

2. Ensure that child resistant closures are used for bottles intended to be a "unit of use" (e.g. 30 tablets, 90 tablets) to be in accordance with the Poison Prevention Act.

C. SAMPLE BLISTER LABELING

1. See General Comment A.1.

2. The established name is presented with the active ingredients joined by a plus sign (+). For consistency throughout the labeling, please remove the plus sign and replace with the word "and".

3. Each individual blister should contain the proprietary name, established name, product strength, lot number and expiration date in case the blister is separated from the sample blister carton or cut into single tablets.

D. SAMPLE CARTON LABELING

1. See General Comment A.1.

2. See Sample Blister Labeling Comment C.2.

E. PACKAGE INSERT LABELING

No comments at this time.

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Appendix A – DMETS Prescription Study Results for Duetact

Inpatient	Outpatient	Voice
Duetact	Duetart	Dutax
Dretact	Duotact	Dutass
Duetact	Duitaid	Dutast
Duetact	Dutlut	D-pack
Duretact	Ditelath	Detast
Duetact	Duetait	Dutask
Dietact or Duetact	Duetatic	Utak
Duetact	Dustart	Dutass
Duetact	Duetart	Dutat or Dutact
Duetact	Duelait	Dutask
Duetact	Dnetath	Dutact
Dietact	Duclact	Butat
Dietact	Duetast	Dietact
Dietact	Duetart	Duetact
Dretact	Duitait	
Duetact	Duitartl	
Duetact	Duetart	
Duetact	Duelate	
Duetact	Duetact	
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