

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-187

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mailstop 4447)**

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TO: Debra B. Birnkrant, MD
Director, Division of Anti-Viral Products
HFD-530

THROUGH: Todd Bridges, RPh, TeamLeader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Deveonne Hamilton-Stokes, RN, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: Intelence
(Etravirine) Tablets
100 mg

NDA/IND # 22-187/63,646

SPONSOR: Tibotec, Inc.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Intelence. This is considered a final decision. However, if 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, Intelence, acceptable from a promotional perspective.

We would be willing to meet with the Division for further discussion, if needed. Please copy DMETS on any correspondence to the sponsor pertaining to this review. DMETS would appreciate feedback of the final outcome of this consult. If you have further questions or need clarifications, please contact OSE Project Manager, Anne Crandall, at 301-796-2282.

**Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
White Oak Bldg #22, Mailstop 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: June 29, 2007

NDA/IND #: 22-187/63,646

NAME OF DRUG: Intelence
(Etravirine) Tablets
100 mg

NDA HOLDER: Tibotec, Inc.

I. INTRODUCTION:

This review was written in response to a request from the Division of Anti-viral Products (HFD-530), for an assessment of the proprietary name "Intelence" regarding potential name confusion with other proprietary or established drug names. Container label and insert labeling were provided for review and comment at this time.

PRODUCT INFORMATION

Intelence (Etravirine) is being developed for the treatment of human immunodeficiency virus type 1 (HIV) infection in antiretroviral treatment-experienced adult patients. Intelence will be available in 100 mg tablets. The recommended dose is 200 mg twice daily. Intelence is to be co-administered with other antiretroviral agents.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to "Intelence" 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 conducted⁵. The Saegis⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel

¹ MICROMEDEX Integrated Index, 2007, 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, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

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. Following completion of these initial components, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Intelence. 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 finds the proprietary name, Intelence, acceptable from a promotional perspective.
2. The Expert Panel identified sixteen proprietary names that were thought to have the potential for confusion with Intelence. The names are as follows: Intellectol, Intestive, Embeline, Invirase, Intensol, Entecavir, Interex, Inderide, Integrelin, Insulin, Intestra, Intelert, Lotensin, Ellence, Intal and Intellan. An independent review identified Isentress as having look-alike similarities with Intelence. In addition, three members of the panel felt it looked and/or sounded like the word "intelligence".

B. PRESCRIPTION STUDY ANALYSIS

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 Intelence 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 123 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 Intelence (see page 4). 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
<p><u>Outpatient RX:</u> <i>Intelence 100mg #240</i> <i>Sig: 2 tabs po BID pc</i></p>	<p>Intelence 100 mg #240 tablets Take 2 tablets twice a day following meals</p>
<p><u>Inpatient RX:</u> <i>Intelence 100mg 2 tablets po BID after meals</i></p>	

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 (page 7) for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Intelence, seventeen proprietary names were identified as having a similar appearance or sound to Intelence. These names are: Intellectol, Intestive, Embeline, Invirase, Intensol, Entecavir, Interex, Inderide, Integrelin, Insulin, Intestra, Intelert, Lotensin, Ellence, Intal, Intellan and Isentress. Additionally, the word "intelligence" was thought to have the potential for confusion.

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, Intelence.

Upon initial analysis, ten of the seventeen names were not considered further due to the lack of significant look-alike and/or sound alike similarities to Intelence in addition to having numerous differentiating product characteristics that may include: indication for use, product strength, usual dosage, route of administration, frequency of administration, therapeutic class, unit of measure, dosage form, prescriber population, patient population, product unavailability and/or area of marketing. These ten names include: Embeline, Intensol, Entecavir, Insulin, Inderide, Integrelin, Lotensin, Intestra, Intelert and Intal. Additionally, the word "intelligence" was not considered further because we believed it to lack convincing orthographic or phonetic similarities to Intelence and we cannot foresee a clinical situation in which the two names would be confused.

The remaining seven (n=7) names, Invirase, Intestive, Intelectol, Interex, Ellence, Intellan and Isentress, were reviewed in depth because of their increased orthographic/phonetic similarity and potential overlapping product characteristics. Upon further analysis, these seven names were assessed as having minimal risk of confusion because of the differentiating product characteristics listed in the "Reason for Discard" column in Table 1 below. Thus DMETS finds the name, Intellece, acceptable.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Reason for Discard				
Invirase	Saquinavir Mesylate Capsules: 200 mg Tablets : 500 mg	1000 mg twice a day in combination with ritonavir 100 mg twice a day; should be taken within 2 hours after a meal	LA	<ul style="list-style-type: none"> Available in multiple strengths (200 mg, 500 mg vs. 100 mg) Usual dose (1000 mg vs. 200 mg) The upstroke "p" and "q" in Intellece are prominent and help to differentiate the name
Intestive	Dietary supplement Capsules: 500 mg	Take four to six capsules a day	LA	<ul style="list-style-type: none"> Strength (500 mg vs. 100 mg) Usual dose (4 to 6 capsules vs. 200 mg) Indication of use (dietary supplement vs. treatment of HIV) Frequency of administration (daily vs. twice a day) Prescription status (over-the-counter vs. prescription)
Intelectol	Dietary supplement Vinpocetine Tablets: 10 mg	Take 2 tablets twice daily with meals	LA	<ul style="list-style-type: none"> Indication of use (dietary supplement vs. treatment of HIV) The endings of each name are distinct (-ctol vs. -nce) Prescription status (over-the-counter vs. prescription)
Interex	Herbal supplement Forskolin Capsules	100 mg to 300 mg/day of an extract containing 10 % to 20 % forskolin	LA	<ul style="list-style-type: none"> Indication of use (herbal supplement vs. treatment of HIV) Usual dose (100 mg to 300 mg vs. 200 mg) Prescription status (over-the-counter vs. prescription) The endings of each name are distinct (-rex vs. -lence) The upstroke letter "l" in Intellece is prominent Product unavailability
Ellence	Epirubicin hydrochloride Injection: 2 mg/mL	100 mg/m ² to 120 mg/m ² in three to four week cycles	LA/SA	<ul style="list-style-type: none"> Strength (2 mg/mL vs. 100 mg) Frequency of administration (3 to 4 week cycles vs. twice a day) Dosage form (injection vs. tablets) Indication of use (adjuvant treatment of breast cancer vs. treatment of HIV) Route of administration (intravenously vs. orally) The first syllable "in" in Intellece helps to distinguish the name

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Proprietary Name	Established Name	Usual Adult Dosage	Similarity	Reason for Similarity
Intellan	Herbal supplement Capsule, Syrup	1 capsule twice a day after meals 2 teaspoons twice a day after meals Duration of 3 months; for long term therapy a gap of three weeks is advised after each three period treatment	LA/SA	<ul style="list-style-type: none"> • Indication of use (herbal supplement vs. treatment of HIV) • Available in multiple dosage forms (capsule, syrup vs. tablets) • Prescription status (over-the-counter vs. prescription) • Usual dose (1 capsule or 2 teaspoons vs. 200 mg) • Duration of treatment (3 months; for long term therapy a gap of three weeks is advised after each three period treatment vs. ongoing)
Isentress	Raltegravir potassium Tablets: 400 mg	400 mg twice a day	LA	<ul style="list-style-type: none"> • Lacks convincing orthographic similarities • Strength (400 mg vs. 100 mg) • Usual dose (400 mg vs. 200 mg)
<p>*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)</p>				

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III. LABELING, PACKAGING AND SAFETY RELATED ISSUES:

In the review of the container label and insert labeling of Intelence, DMETS focused on safety issues relating to medication errors. However, DMETS could not comment with completeness on the label and labeling without the final copies marked with the proposed proprietary name, Intelence. DMETS has identified the following areas of improvement, which may minimize potential user error and maximize patient safety.

A. CONTAINER LABEL

1. The established name should be at least ½ the size of the proprietary name per 21 CFR 201.10 (g)(2).
2. Delete the statement “Each tablet contains 100 mg of etravirine”, as it is redundant since the strength and established name already appear on the label.
3. At the end of the ALERT statement, add the phrase “... from your healthcare provider”, to ensure patients know where to find this essential information.
4. Since the bottles are unit-of-use, ensure they have child-resistance caps (CRC) to be in compliance with the Poison Prevention Act.
5. We note there is a rectangle graphic at the bottom of the principle display panel. DMETS questions what will be printed here and if the graphic will compete or deter from the readability of the proprietary and established names and strength.

B. PACKAGE INSERT LABELING

DMETS does not recommend the use of the abbreviation — We recommend writing out the full word “kilocalorie” throughout the package insert. FDA and Institute for Safe Medication Practices (ISMP) launched a campaign on June 14, 2006, warning health care providers and consumers not to use error-prone abbreviations, acronyms, or symbols. Thus, we request that the Divisions not approve or use such abbreviations in labels and labeling.

C. PATIENT INSERT LABELING

No Comments at this time.

**APPEARS THIS WAY
ON ORIGINAL**

Appendix A: Prescription Study Results for Intelence

Inpatient	Outpatient	Verbal
Intelence	Intelence	Atalence
Intelence	Intelence	Intalents
Intelence	Intelence	Intelligence
Intelence	Intelence	Intelance
Intelence	Intelence	Intela
Intelence	Intelence	Intellits
Intelence	Intelence	Intelants
Intelence		Etalence
Intelence		Intelligence
		Talents
		Talon

**This is a representation of an electronic record that was signed electronically and
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/s/

Deveonne Hamilton-Stokes
12/5/2007 04:50:31 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
12/6/2007 10:40:41 AM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, DMETS Director