

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-998

PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

Date: May 1, 2009

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Subject: Proprietary Name Review

Drug Name(s): Plan B One-Step (Levonorgestrel) Tablet, 1.5 mg

Application Type/Number: NDA 21-998

Applicant/sponsor: Duramed

OSE RCM #: 2009-755

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EXECUTIVE SUMMARY

This review was written in response to receipt of an April 21, 2009 request for review of the proprietary name Plan B One-Step. This submission was made at the request of the FDA following discussion with the applicant on April 20, 2009 when we objected to the use of the proposed proprietary name Plan B _____ for the reasons outlined in the discussion (see section II) of this document. The proposed proprietary name Plan B One-Step is acceptable to the FDA for the proposed product. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

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1 BACKGROUND

Plan B is the proprietary name of an approved drug product (levonorgestrel 0.75 mg tablets). The product was first approved on July 28, 1999 as a prescription only drug intended to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse. Plan B subsequently received approval on August 24, 2006 for over-the-counter (OTC) use in women 18 years of age and older. For women 17 years of age and younger, the product is currently available only via prescription.¹ The product is administered as a two-tablet regimen. The first tablet is to be taken orally as soon as possible within 72 hours of intercourse; the second tablet is to be taken 12 hours after the first dose. To manage a product with both prescription and non-prescription status, pharmacies keep the product "behind the counter" to ensure that it is dispensed without a prescription only to women 18 years of age and older.

Watson Laboratories, Inc. has submitted two applications for a generic version of Plan B. These applications, _____ ANDA 78-665, are currently being reviewed within FDA. Watson Laboratories, Inc. is seeking approval for both applications by August 2009 when the exclusivity of the innovator drug, Plan B will expire.

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The holder of the application for Plan B, Duramed, has submitted a New Drug Application for a new formulation of the product. This new formulation will be a single tablet containing 1.5 mg levonorgestrel. This product is to be administered as a single dose. Duramed has submitted for review the proposed proprietary name "Plan B _____" for this product. The features of these products are summarized in Table 1 below.

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Table 1: Product Characteristics

Product	Package Size	Strength	Drug Class	Directions for Use
Plan B (levonorgestrel) NDA 21-045 currently marketed	2 tablet blister pack	0.75 mg tablets	Rx/OTC	One tablet within 72 hours after exposure followed by the second tablet 12 hours after initial dose
Levonorgestrel Generic Product pending approval	2 tablet blister pack	0.75 mg tablets	Rx/OTC	One tablet within 72 hours after exposure followed by the second tablet 12 hours after initial dose
Plan B _____ (levonorgestrel) NDA 21-998 To be marketed	1 tablet blister pack	1.5 mg tablet	Rx/OTC	One tablet within 72 hours after exposure

¹ On March 23, 2009, the US District Court in Washington DC order FDA to allow Plan B to be available to women age 17 years and older without a prescription. Our analysis of the proposed proprietary name _____ applies regardless of the age range for which Plan B is available without a prescription.

2 DISCUSSION

The holder of the application for Plan B, Duramed, submitted a New Drug Application for a new formulation of the product on January 24, 2006. On January 8, 2009, Duramed submitted for review the proposed proprietary name "Plan B" for this product. b(4)

During our review the following concerns were raised if both the generic formulation of Plan B (levonorgestrel 0.75 mg) and the new formulation (levonorgestrel 1.5 mg) are approved:

- Confusion may occur between Plan B and Plan B when prescribed on a prescription. According to Duramed's proprietary name submission for Plan B, the currently marketed Plan B product will be discontinued. There will be a transition period of about two weeks, during which Plan B and the new single-dose formulation will co-exist in the market, a condition with potential for dispensing and prescribing errors among the Plan B product line. b(4)
- The arrival of a generic formulation of Plan B (anticipated in or after August 2009) will create a situation under which the levonorgestrel 0.75 mg tablet could be inappropriately substituted for the levonorgestrel 1.5 mg product. ONP and Duramed indicated this was a concern.

DMEPA objected to the proposed proprietary name "Plan B" because we did not believe it would minimize either of the primary concerns listed above. The proposal to use the modifier "1" is inherently error prone for the following reasons: b(4)

- The modifier "1" is ambiguous by itself. The ambiguity of the numeric suffix stems from the fact that the number lacks a descriptor that would provide a standard meaning allowing for a consistent interpretation. This is problematic because Plan B will be available by prescription as well as without a prescription. Because of this dual marketing status, we are forced to consider how the proposed product name could be interpreted when written on a prescription, even if the amount of product dispensed via prescription is low compared to non-prescription distribution. b(4)

Numerical modifiers without descriptors have led to misinterpretation in the prescription realm. Postmarketing examples include:

Viokase 8 – This product is used to aid in digestion and is composed of 30,000 units of amylase, 8,000 units of lipase, and 30,000 units of protease. The dosing is based on the amylase component. The modifier "8" was intended to indicate the 8,000 units of lipase. However, this name when written on a prescription was misinterpreted to mean the number of capsules to administer rather than the intended strength. This resulted in the patient administering 8 capsules.

Percocet 5 – When Percocet was first approved the modifier 5 was used to indicate the strength of the tablet. However, on prescription the number 5 was misinterpreted as the number of tablets to dispense and/or number of tablets to administer. Additionally, when further strengths were proposed (i.e., 2.5 mg, 7.5 mg, and 10 mg of oxycodone) DMEPA did not allow the use of a single number in the proprietary name and agreed on the use of both active ingredient strengths for product identification (e.g. Percocet 5/325, etc.).

Since Plan B and Plan B (including its generic formulation) will be available as a prescription product, the same type of misinterpretation might occur as exemplified above. In this case, the number "1" could be misinterpreted to mean one box, one dose of the 0.75 mg box, or one tablet of either the 0.75 mg or 1.5 mg levonorgestrel tablet. Thus, the inclusion of the number "1" as a modifier without a descriptor is ambiguous and may actually contribute to generic substitution of the unintended formulation or incorrect dosing of the currently marketed levonorgestrel 0.75 mg product. b(4)

- Approval of Plan B — would set an unwanted precedent of numbers without qualification being used as modifiers in proprietary names of prescription drugs. Given the fact that a written or oral communication of the name is necessary to dispense a prescription, any ambiguity in meaning of a proposed numerical modifier may lead to misinterpretation. This concern is based on our experience reviewing reports of postmarketing reports of medication error confusion with numerical modifiers that are not qualified in some way. When numeric modifiers have been allowed for prescription products a qualifier is appended to the number (i.e., 24-hour, 12-hour or 300 mg/30 mg). In these instances the qualifier placed next to the number clearly conveys a single meaning of either dosing interval or product strength, respectively. Additionally, OSE is striving to be consistent with the recommendations set forth in the 2006 IOM report entitled "Preventing Medication Errors" in which it was recommended that FDA standardize modifiers to the extent possible. As part of good naming practices, OSE is attempting to critically review the use of modifiers and approve only those proprietary names with modifiers that are not ambiguous or open to multiple interpretations. Allowing the use of the word — as a modifier would set a precedent that goes against our attempts to address the ongoing confusion seen postmarketing with this type of nomenclature with prescription medicines.

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Additionally, because of the dual marketing status, there is also a risk that the modifier will be omitted from the prescription or the product may be ordered by the established name alone, leaving only the product strength to differentiate the two products. It was for these reasons that OSE initially recommended the product retain the Plan B name (without any modifier) and be differentiated by strength alone. However, ONP is concerned that because these products are or will be available without a prescription, the use of a modifier is necessary to allow consumers to differentiate between the 0.75 mg formulation and the 1.5 mg formulation. We agree with this assessment. However, we contend that this product is different than most non-prescription medications because of the dual marketing status. These, currently, are not self selected by consumers, but rather stored behind the pharmacy counter. If, however, these products will be available without a prescription, as standard over-the-counter products, we align with ONP's assessment that a modifier would be helpful to the consumer in differentiating between the two products since this is a common nomenclature practice among OTC products. However, the number "One" without a descriptor will not address this issue without causing the confusion noted above.

We concluded that an alternative name consist of "Plan B' followed by a non-ambiguous modifier. On April 20, 2009, a teleconference was held with the sponsor to discuss FDA's objection to the proposed name. During this teleconference FDA and the sponsor reached consensus that Plan B — would be withdrawn from consideration and that FDA would accept an alternate name Plan B One-Step.

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