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RESEARCH**

APPLICATION NUMBER:

21-998

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-998

NDA APPROVAL

Duramed Pharmaceuticals, Inc.
Attention: Michele G. Walsh
Director, Clinical Regulatory Affairs
One Belmont Avenue, 11th Floor
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

Please refer to your new drug application (NDA) dated and received January 24, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plan B[®] One-Step (levonorgestrel) tablet, 1.5 mg.

We acknowledge receipt of your submissions dated February 23, March 2 and 20, June 20 and 29, July 14, August 16, September 26 and 27, October 13 and 19, November 3 (2), 8 (2), 9, 21, and 29, 2006, October 14, 2008, January 8 and 9, February 12, March 12, April 20 (2) and 28 (2), May 19, June 9 (2), 22, 25, 26, and 30, and July 1, 7 (2), 8 (3), and 9, 2009.

The January 9, 2009, submission constituted a complete response to our November 22, 2006, action letter.

This new drug application provides for:

1. Over-the-counter (OTC) availability of Plan B[®] One-Step for women age 17 years and older. Plan B[®] One-Step reduces the chance of pregnancy after unprotected sex (if a contraceptive failed or if you did not use birth control).
2. Prescription availability of Plan B[®] One-Step for women younger than age 17 years. Plan B[®] One-Step is emergency contraception for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text (prescription package insert, carton label, inner blister card label, and consumer information leaflet).

PRESCRIPTION CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the prescription content of labeling [21 CFR 314.50(f)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling text for the package insert (submitted July 9, 2009). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-998."

OTC CONTENT OF LABELING

Submit final printed labeling as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the enclosed labeling (consumer information leaflet submitted July 8, 2009).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels identical to the enclosed labeling (carton label and inner blister card label submitted July 8, 2009) as soon as they are available, but no more than 30 days after they are printed. These must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

Please submit the labels and the OTC content of labeling electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "Final Printed Carton and Container Labels for approved NDA 21-998." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

We remind you to remove the "NEW! Now only ONE dose" flag from the principal display panel after six months of marketing.

CARESM PROGRAM

We also acknowledge receipt of your submission dated July 7, 2009, describing the modified CARESM Program (see enclosure) that you will apply to Plan B[®] One-Step.

You must discuss any change to the CARESM Program with the FDA prior to implementation of the change.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for premenarcheal patients because premenarcheal patients are not at risk of becoming pregnant and the use of this product before menarche is not indicated. We note that you have fulfilled the pediatric study requirement for postmenarcheal pediatric patients.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Pamela Lucarelli, Regulatory Health Project Manager, at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Scott Monroe, M.D.
Director
Division of Reproductive and
Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

{See appended electronic signature page}

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical
Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

Enclosures

DURAMED PHARMACEUTICALS, INC.

CARESM (CONVENIENT ACCESS, RESPONSIBLE EDUCATION) PROGRAM

THE MARKETING, EDUCATION, DISTRIBUTION, AND MONITORING PROGRAM FOR PLAN B[®] ONE-STEP

Introduction

The CARESM (Convenient Access, Responsible Education) Program was carefully constructed in 2006 to help ensure that Plan B[®] will be used responsibly and appropriately. The CARESM Program is now being extended to the new product Plan B[®] One-Step. The focus of CARESM will shift to Plan B[®] One-Step following its approval and launch, and the corresponding cessation of distribution of Plan B[®] and a transition to Plan B[®] One-Step in the marketplace.

Plan B[®] One-Step is an over-the-counter (OTC) product for women age 17 or older, with a prescription-only requirement for women younger than age 17. The sales and marketing plan for Plan B[®] One-Step has been designed to limit the availability of this product, to the extent practical, to pharmacies and clinics, and to educate healthcare professionals and consumers within the target age groups regarding the responsible use of Plan B[®] One-Step. The need to take Plan B[®] One-Step in as timely a manner as possible dictates that any responsible marketing program not only address healthcare professionals but also include extensive consumer education which includes a direct access component as a means of gaining such information. Thus, the CARESM program contains elements that include an appropriate consumer education component. In addition, the sponsor will work closely with retail pharmacies and drug wholesalers to ensure that they will carry Plan B[®] One-Step and that they will understand and follow the prescription age requirement for the dispensing of the product to women younger than age 17.



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CARESM Program**

The CARESM program is intended to address issues affecting access to Plan B[®] One-Step by providing sources of accurate and responsible information to both healthcare providers and consumers. It is also designed to provide a framework for pharmacies to ensure availability of Plan B[®] One-Step as an OTC product when sought by knowledgeable consumers who are 17 years or older. Women younger than age 17 will require a prescription from their healthcare provider in order to obtain Plan B[®] One-Step. The CARESM program is not intended to impact or change those who can lawfully prescribe or dispense Plan B[®] One-Step under prevailing state laws.

Four core elements of CARESM contribute to the achievement of program objectives.

- **Labeling/Packaging/Informational toll free number** (to provide essential information to consumers in an accessible, easy to understand format. The Plan B[®] One-Step packaging is designed to meet both prescription and OTC requirements.)
- **Education** (to provide information intended to educate physicians, pharmacists, pharmacy staff, nurse practitioners, and patients. Educational initiatives will focus on clearly instructing all audiences on the new dosing regimen of a single tablet, and the new lower age requirement that women younger than age 17 obtain a prescription for Plan B[®] One-Step.)
- **Distribution** (to ensure that Plan B[®] One-Step will be available only to licensed drug wholesalers, retail operations with pharmacy services and clinics with licensed healthcare practitioners, and to successfully facilitate the Plan B[®] One-Step prescription-only age requirement. These settings will also provide easy access by the consumer to a pharmacist or other healthcare professional should questions arise.)
- **Monitoring** (to evaluate the effectiveness of the program by determining if the age restriction is understood by all audiences and is properly being adhered to.)



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I. Labeling/Packaging

The Plan B[®] One-Step labeling was developed to provide clear and comprehensive communication of the key messages outlined above, and to make known additional sources of information. The Plan B[®] One-Step packaging is designed to meet all requirements of both a prescription and over-the-counter product. It is consistent with that used for Plan B[®]. The Plan B[®] One-Step packaging will allow pharmacies to appropriately dispense Plan B[®] One-Step as either a prescription or OTC product. The package also provides educational information to the consumer in a patient friendly format.

Elements of the package are as follows:

- The back of the carton includes the Drug Facts as well as a space for the pharmacy to place the required prescription labeling;
- The statement, "Rx only for women younger than age 17" appears on the Principal Display Panel and "prescription only for women younger than age 17. If you are younger than age 17, see a healthcare professional" appears on the Drug Facts panel of the carton;
- The inner portion of the carton houses the Plan B[®] One-Step tablet and clearly states the directions for when to take Plan B[®] One-Step;
- The Plan B[®] One-Step Package Insert and an educational booklet designed for the consumer (Consumer Information Leaflet) will be housed inside the carton;



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- The toll-free number for the Plan B[®] One-Step 24-hour Information Line and the Plan B[®] One-Step web address are clearly displayed in the Drug Facts panel of the package should the consumer have additional questions on Plan B[®] One-Step.

II. Education

The CARESM Program provides for an intensively educational approach to the introduction of Plan B[®] One-Step as a single tablet dosing regimen that is available OTC to those age 17 years or older. Educational programs will focus on both healthcare professionals as well as consumers. The consumer advertising is designed to stimulate discussions with healthcare providers. The program will assist healthcare providers in developing an adequate knowledge base so that they can provide responsible and accurate counseling to patients.

Efforts directed to raising consumer awareness of the product and its appropriate use will follow appropriate professional education programs. The educational materials will address not only Plan B[®] One-Step but will encourage healthcare professionals to urge users to adopt routine forms of contraception and avoid reliance on Plan B[®] One-Step as their primary form of birth control.

A. Educational Program to Healthcare Professionals.

Plan B[®] One-Step will be introduced and explained to healthcare professionals to raise awareness and knowledge levels as to this product for emergency contraception. This program is intended to ensure that healthcare professionals are prepared to support their patient populations.

Specifically, the new dosing regimen of a single tablet, and the new lower prescription age requirement will be emphasized to healthcare professionals to ensure that they are knowledgeable of the prescription requirement for women



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younger than age 17, and that they understand how to appropriately dispense the Plan B[®] One-Step package in both prescription and OTC scenarios.

Continuing Education programs will be initiated for pharmacists, as was done at the time Plan B[®] was made available as a dual-labeled Rx/OTC product. The sponsor's sales representatives¹ will communicate the prescription requirement for women younger than age 17, as well as the OTC availability of Plan B[®] One-Step for those 17 years of age or older.

B. Educational Campaign to Consumers

The consumer education campaign is anticipated to begin immediately following the approval of Plan B[®] One-Step, in order to avoid confusion regarding the new lower prescription age requirement and the new dose regimen.

1. The campaign will be designed to convey critical awareness and educational messages as well as information about product availability, the time sensitivity of use, and the age requirements to obtain Plan B[®] One-Step as a prescription or OTC product. The intent will be to make consumers aware of the availability of emergency contraception, its appropriate use and the need to use it as soon as possible. Women younger than age 17 will be encouraged to contact their healthcare professional to learn about emergency contraception, routine forms of birth control, and sexually transmitted infection (STI)/human immunodeficiency virus (HIV).
2. The direct to consumer campaign will be designed to target those ages 17 to 44.
 - i) The language and visuals used will be appropriate and of interest to this

¹ The sponsor's sales force for female healthcare products, currently consisting of approximately 230 sales representatives, visit the offices of approximately 30,000 physicians, mostly Obstetricians and Gynecologists.



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targeted age group. As appropriate, new promotional materials will be provided to FDA for comment. Promotional materials will be submitted to the Division of Drug Marketing, Advertising, and Communications via Form FDA 2253.

- ii) Media placements that target audiences younger than age 17 will not be used.

III. Distribution

The sponsor believes that in the interest of responsible usage (and in recognition of the circumstances of the need for emergency contraception), Plan B[®] One-Step should be available in those retail pharmacy outlets that typically sell a broad range of OTC medications and that have pharmacy services staffed with pharmacists (or, in the case of clinics, other healthcare professionals) during normal business hours to answer questions. Since Plan B[®] One-Step will have a prescription only requirement for women younger than age 17, Duramed Pharmaceuticals and the third party distributors, wholesaler distribution and chain drug companies, will only be allowed to distribute Plan B[®] One-Step to licensed pharmacies or other licensed healthcare clinics, as it would be unlawful to distribute a prescription product to any business that does not have a valid pharmacy license and/or physician license. As with Plan B[®], since Plan B[®] One-Step has both Rx and OTC labeling, it will be treated as any other Rx product for distribution purposes; specifically, it would only be distributed to licensed pharmacies or healthcare clinics. Therefore, Plan B[®] One-Step will not be available at gas stations or convenience stores. Additionally, since Plan B[®] One-Step has both Rx and OTC labeling, the pharmacies will keep the product behind the counter and control it as an Rx product. The pharmacy and clinic settings will also allow pharmacists and other healthcare providers to properly restrict OTC access to those age 17 years or older.



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IV. Monitoring

The sponsor intends to monitor trends in the use of emergency contraception to evaluate the effectiveness of the CARESM program and will make adjustments as appropriate. Monitoring will be accomplished in several ways, with information gathered from both healthcare professionals and consumers.

Monitoring actual use of Plan B[®] One-Step is complex due to the difficulties inherent in identifying those who have purchased the product and in gathering useful, generalizable information. Consequently, the monitoring component will rely on a variety of sources intended to provide trend data, observational data, and signals of program effectiveness and potential problems. Monitoring components may include the following:

1. A market research survey or surveys of a subset of healthcare professionals (e.g. OB/GYN, family practice, pharmacists, nurses, family planning and health clinic personnel) to determine:
 - Whether the prescription requirement for women younger than age 17 is understood and is being adhered to at the point of purchase
 - Attitudes toward and experience with patients' usage of Plan B[®] One-Step
 - Trends among emergency contraception users within their patient population (especially source of awareness, repeat use, use instead of more effective forms of contraception, incidence of STIs, etc.)
 - Nature of interactions with Plan B[®] One-Step users (Does the contact with the healthcare professional occur prior to product usage? after usage? Are the women in search of contraceptive counseling? What



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types of side effects are being seen in use?)

- Areas where additional information is needed in the marketplace, as identified by the questions raised by the users

2. Gathering data from actual users of Plan B[®] One-Step is difficult because the number of users will be relatively small and because the decision to use emergency contraception is a private and emotional one. Women choosing to use the product are expected to wish to remain anonymous and are entitled to maintain their privacy. Nevertheless, the sponsor may work with a variety of sources in an effort to obtain and analyze consumer data in accordance with HIPAA regulations to assess the effectiveness of the CARESM program elements.

3. Monitoring compliance of the Plan B[®] One-Step prescription age requirement can be somewhat complex because there will be no documented information on the purchasers of Plan B[®] One-Step who were old enough to obtain it as an OTC product. The Sponsor intends to monitor the level of comprehension of the prescription age requirement particularly at the pharmacy level, where the age of consumers must be assessed at the point of purchase. The following program will provide accurate information directly related to accessing compliance:

- **Point of Purchase Monitoring Program:**

The Sponsor will continue to conduct a "Point-of-Purchase Monitoring Program", which intends to track how Plan B[®] One-Step is being sold at the time of purchase. Due to the challenges of obtaining specific purchase data on an OTC product and respecting consumer privacy, this program will include anonymous shoppers who will be directed to visit locations where Plan B[®] One-Step is available and purchase the product. These transactions will be documented and analyzed to determine the level of comprehension



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of the Plan B[®] One-Step prescription age requirement and how it is handled at the point of purchase. The shoppers in this program will be 15 to 16 years old. Parental consent will be obtained for the shoppers as they will be under the age of 18 years. Locations for this program will be selected based on areas where Plan B[®] One-Step use is high, and will be in different regions of the US to provide a national representation of the findings. These findings would provide concrete information on how the prescription age requirement for Plan B[®] One-Step is being addressed at the pharmacy and if it is properly being followed. The Sponsor will use these findings to identify areas where more education on the prescription age restriction is needed and will focus their efforts on improving the level of understanding among pharmacists and the pharmacy staff. Findings from the study will be communicated to the pharmacy, and the corporate office, if appropriate, since education and retraining will be the first course of remedial action. In the case of repeat violators, the violator's State Board of Pharmacy will be notified. The Point-of-Purchase Monitoring Program will be conducted annually.

V. Reporting

The sponsor will provide FDA a monitoring report with the available results from the above monitoring activities, including the point of purchase monitoring, on an annual basis, with submission of the report within 60 calendar days after the interval date. Any change in reporting period will be requested by the sponsor and agreed to by FDA.

Duramed Pharmaceuticals, Inc.
July 2009

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

Scott Monroe

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Andrea Segal

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