CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 76-334

Name: Previfem Tablets (Norgestimate and Ethinyl Estradiol Tablets, 0.25 mg/0.035 mg)

Sponsor: Andrx Pharmaceuticals, LLC

Approval Date: January 9, 2004

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-334

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Tentative Approval Letter	
Approved Labeling	X
Labeling Review(s)	X
Medical Review(s)	
Chemistry Reviews	X
Bioequivalence Reviews	X
Statistical Review(s)	
Microbiology Review(s)	
Administrative Documents	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-334

APPROVAL LETTER

ANDA 76-334

JAN 9 2004

Andrx Pharmaceuticals, LLC
Attention: William Stahovec
2945 W. Corporate Lakes Blvd.
Weston, FL 33331

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 27, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Previfem Tablets (Norgestimate and Ethinyl Estradiol Tablets, 0.25 mg/0.035 mg), packaged in 28-day cycle regimens.

Reference is also made to your amendments dated June 27, and July 17, 2002; and May 1, November 12, November 17, December 9, and December 10, 2003.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Previfem Tablets (Norgestimate and Ethinyl Estradiol Tablets, 0.25 mg/0.035 mg) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Ortho Cyclen-28® Tablets, 0.25 mg/0.035 mg, of Ortho McNeil Pharmaceutical, Inc.). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Gary Buehler
Director
1/9/04
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 76-334
Division File
Field Copy
HFD-610/R. West
HFD-330
HFD-205
HFD-610/Orange Book Staff

Endorsements:
HFD-623/R.Trimmer/ 12-30-03
HFD-623/D.Gill/ for 30 Dec 03
HFD-617/S.Park/ for 12/30/03
HFD-613/D.Catterson/ Debra M. Catterson 12/31/03
HFD-613/J.Grace/ 12/31/2003

12/26 and 1/6/04

V:\FIRMSAM\ANDRX\LTRS&REV\76334.AP.doc
F/T by

APPROVAL

Robert Lyn West
1/6/2004
pending DHETS update
of OK for proprietary
name.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-334

APPROVED LABELING

76-334

PREVIFEM™

(norgestimate and ethinyl estradiol)

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

PREVIFEM™ Tablets (norgestimate and ethinyl estradiol): Each blue tablet contains 0.25 mg norgestimate and 0.035 mg ethinyl estradiol. Each teal tablet contains inert ingredients.

BRIEF SUMMARY PATIENT PACKAGE INSERT

Oral contraceptives, also known as "birth control pills" or "the pill," are taken to prevent pregnancy. When taken correctly to prevent pregnancy, oral contraceptives have a failure rate of less than 1% per year when used without missing any pills. The typical failure rate of large numbers of pill users is less than 3% per year when women who miss pills are included. For most women oral contraceptives are also free of serious or unpleasant side effects. However, forgetting to take pills considerably increases the chances of pregnancy.

For the majority of women, oral contraceptives can be taken safely. But there are some women who are at high risk of developing certain serious diseases that can be fatal or may cause temporary or permanent disability. The risks associated with taking oral contraceptives increase significantly if you:

- smoke
- have high blood pressure, diabetes, high cholesterol
- have or have had clotting disorders, heart attack, stroke, angina pectoris, cancer of the breast or sex organs, jaundice or malignant or benign liver tumors.

Although cardiovascular disease risks may be increased with oral contraceptive use after age 40 in healthy, non-smoking women (even with the newer low-dose formulations), there are also greater potential health risks associated with pregnancy in older women.

You should not take the pill if you suspect you are pregnant or have unexplained vaginal bleeding.

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. The risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives are strongly advised not to smoke.

Most side effects of the pill are not serious. The most common such effects are nausea, vomiting, bleeding between menstrual periods, weight gain, breast tenderness, and difficulty wearing contact lenses. These side effects, especially nausea and vomiting, may subside within the first three months of use.

The serious side effects of the pill occur very infrequently, especially if you are in good health and are young. However, you should know that the following medical conditions have been associated with or made worse by the pill:

1. Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), stoppage or rupture of a blood vessel in the brain (stroke), blockage of blood vessels in the heart (heart attack or angina pectoris) or other organs of the body. As mentioned above, smoking increases the risk of heart attacks and strokes and subsequent serious medical consequences.
2. In rare cases, oral contraceptives can cause benign but dangerous liver tumors. These benign liver tumors can rupture and cause fatal internal bleeding. In addition, some studies report an increased risk of developing liver cancer. However, liver cancers are rare.
3. High blood pressure, although blood pressure usually returns to normal when the pill is stopped.

The symptoms associated with these serious side effects are discussed in the **Detailed Patient Labeling.** Notify your doctor or health care provider if you notice any unusual physical disturbances while taking the pill. In addition, drugs such as rifampin, as well as some anticonvulsants and some antibiotics may decrease oral contraceptive effectiveness.

There is conflict among studies regarding breast cancer and oral contraceptive use. Some studies have reported an increase in the risk of developing breast cancer, particularly at a younger age. This increased risk appears to be related to duration of use. The majority of studies have found no overall increase in the risk of developing breast cancer. Some studies have found an increase in the incidence of cancer of the cervix in women who use oral contraceptives. However, this finding may be related to factors other than the use of oral contraceptives. There is insufficient evidence to rule out the possibility that pills may cause such cancers.

Taking the combination pill provides some important noncontraceptive benefits. These include less painful menstruation, less menstrual blood loss and anemia, fewer pelvic infections, and fewer cancers of the ovary and the lining of the uterus.

Be sure to discuss any medical condition you may have with your health care provider. Your health care provider will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be delayed to another time if you request it and the health care provider believes that it is a good medical practice to postpone it. You should be reexamined at least once a year while taking oral contraceptives. The **Detailed Patient**

PREVIFEM™

(norgestimate and ethinyl estradiol)

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

PREVIFEM™

(norgestimate and ethinyl estradiol)

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DETAILED PATIENT LABELING

PLEASE NOTE: This labeling is revised from time to time as important new medical information becomes available. Therefore, please review this labeling carefully.

PREVIFEM™ Tablets: Each blue tablet contains 0.25 mg norgestimate and 0.035 mg ethinyl estradiol. Each teal tablet contains inert ingredients.

INTRODUCTION

Any woman who considers using oral contraceptives (the birth control pill or the pill) should understand the benefits and risks of using this form of birth control. This patient labeling will give you much of the information you will need to make this decision and will also help you determine if you are at risk of developing any of the serious side effects of the pill. It will tell you how to use the pill properly so that it will be as effective as possible. However, this labeling is not a replacement for a careful discussion between you and your healthcare provider. You should discuss the information provided in this labeling with him or her, both when you first start taking the pill and during your revisits. You should also follow your health care provider's advice with regard to regular check-ups while you are on the pill.

EFFECTIVENESS OF ORAL CONTRACEPTIVES FOR CONTRACEPTION

Oral contraceptives or "birth control pills" or "the pill" are used to prevent pregnancy and are more effective than other non-surgical methods of birth control. When they are taken correctly, the chance of becoming pregnant is less than 1% (1 pregnancy per 100 women per year of use) when used perfectly, without missing any pills. Typical failure rates are actually 3% per year. The chance of becoming pregnant increases with each missed pill during a menstrual cycle.

In comparison, typical failure rates for other non-surgical methods of birth control during the first year of use are as follows:

Implant: <1%

Injection: <1%

IUD: 1 to 2%

Diaphragm with spermicides: 20%

Spermicides alone: 26%

Vaginal sponge: 20 to 40%

Female sterilization: <1%

Male sterilization: <1%

Cervical Cap with spermicides: 20 to 40%

Condom alone (male): 14%

Condom alone (female): 21%

Periodic abstinence: 25%

Withdrawal: 19%

No methods: 85%

WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives are strongly advised not to smoke.

Some women should not use the pill. For example, you should not take the pill if you are pregnant or think you may be pregnant. You should also not use the pill if you have any of the following conditions:

- A history of heart attack or stroke
- Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), or eyes
- A history of blood clots in the deep veins of your legs
- Chest pain (angina pectoris)
- Known or suspected breast cancer or cancer of the lining of the uterus, cervix or vagina
- Unexplained vaginal bleeding (until a diagnosis is reached by your doctor)
- Yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during previous use of the pill
- Liver tumor (benign or cancerous)
- Known or suspected pregnancy

Tell your health care provider if you have ever had any of these conditions. Your health care provider can recommend a safer method of birth control.

OTHER CONSIDERATIONS BEFORE TAKING ORAL CONTRACEPTIVES

Tell your health care provider if you have or have had:

- Breast nodules, fibrocystic disease of the breast, an abnormal breast x-ray or mammogram
- Diabetes
- Elevated cholesterol or triglycerides
- High blood pressure
- Migraine or other headaches or epilepsy
- Mental depression
- Gallbladder, heart or kidney disease
- History of scanty or irregular menstrual periods

Women with any of these conditions should be checked often by their health care provider if they choose to use oral contraceptives.

Also, be sure to inform your doctor or health care provider if you smoke or are on any medications.

RISKS OF TAKING ORAL CONTRACEPTIVES

1. Risk of Developing Blood Clots

Blood clots and blockage of blood vessels are one of the most serious side effects of taking oral contraceptives and can cause death or serious disability. In particular, a clot in the legs can cause thrombophlebitis and a clot that travels to the lungs can cause a sudden blocking of the vessel carrying blood to the lungs. Rarely, clots occur in the blood vessels of the eye and may cause blindness, double vision, or impaired vision.

If you take oral contraceptives and need elective surgery, need to stay in bed for a prolonged illness or have recently delivered a baby, you may be at risk of developing blood clots. You should consult your doctor about stopping oral contraceptives four weeks before surgery and not taking oral contraceptives for two weeks after surgery or during bed rest. You should also not take oral contraceptives soon after delivery of a baby. It is advisable to wait for at least four weeks after delivery if you are not breast feeding or four weeks after a second trimester abortion. If you are breast feeding, you should wait until you have weaned your child before using the pill. (See also the section on **Breast Feeding** in **GENERAL PRECAUTIONS**.)

The risk of circulatory disease in oral contraceptive users may be higher in users of high-dose pills and may be greater with longer duration of oral contraceptive use. In addition, some of these increased risks may continue for a number of years after stopping oral contraceptives. The risk of abnormal blood clotting increases with age in both users and nonusers of oral contraceptives, but the increased risk from the oral contraceptive appears to be present at all ages. For women aged 20 to 44 it is estimated that about 1 in 2,000 using oral contraceptives will be hospitalized each year because of abnormal clotting. Among nonusers in the same age group, about 1 in 20,000 would be hospitalized each year. For oral contraceptive users in general, it has been estimated that in women between the ages of 15 and 34 the risk of death due to a circulatory disorder is about 1 in 12,000 per year, whereas for nonusers the rate is about 1 in 50,000 per year. In the age group 35 to 44, the risk is estimated to be about 1 in 2,500 per year for oral contraceptive users and about 1 in 10,000 per year for nonusers.

2. Heart Attacks and Strokes

Oral contraceptives may increase the tendency to develop strokes (stoppage or rupture of blood vessels in the brain) and angina pectoris and heart attacks (blockage of blood vessels in the heart). Any of these conditions can cause death or serious disability.

Smoking greatly increases the possibility of suffering heart attacks and strokes. Furthermore, smoking and the use of oral contraceptives greatly increase the chances of developing and dying of heart disease.

Oral contraceptive users probably have a greater risk than nonusers of having gallbladder disease although this risk may be related to pills containing high doses of estrogens.

4. Liver Tumors

In rare cases, oral contraceptives can cause benign but dangerous liver tumors. These benign liver tumors can rupture and cause fatal internal bleeding. In addition, some studies report an increased risk of developing liver cancer. However, liver cancers are rare.

5. Cancer of the Reproductive Organs and Breasts

There is conflict among studies regarding breast cancer and oral contraceptive use. Some studies have reported an increase in the risk of developing breast cancer, particularly at a younger age. This increased risk appears to be related to duration of use. The majority of studies have found no overall increase in the risk of developing breast cancer.

A meta-analysis of 54 studies found a small increase in the frequency of having breast cancer diagnosed for women who were currently using combined oral contraceptives or had used them within the past ten years. This increase in the frequency of breast cancer diagnosis, within ten years of stopping use, was generally accounted for by cancers localized to the breast. There was no increase in the frequency of having breast cancer diagnosed ten or more years after cessation of use.

Some studies have found an increase in the incidence of cancer of the cervix in women who use oral contraceptives. However, this finding may be related to factors other than the use of oral contraceptives. There is insufficient evidence to rule out the possibility that pills may cause such cancers.

ESTIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY

All methods of birth control and pregnancy are associated with a risk of developing certain diseases, which may lead to disability or death. An estimate of the number of deaths associated with different methods of birth control and pregnancy has been calculated and is shown in the following table.

ANNUAL NUMBER OF BIRTH-RELATED OR METHOD-RELATED DEATHS ASSOCIATED WITH CONTROL OF FERTILITY PER 100,000 NON-STERILE WOMEN, BY FERTILITY CONTROL METHOD ACCORDING TO AGE

Method of control and outcome	15-19	20-24	25-29	30-34	35-39	40-44
No fertility control methods*	7.0	7.4	9.1	14.8	25.7	28.2
Oral contraceptives Non-smoker**	0.3	0.5	0.9	1.9	13.8	31.6
Oral contraceptives Smoker**	2.2	3.4	6.6	13.5	51.1	117.2
IUD**	0.8	0.8	1.0	1.0	1.4	1.4
Condom*	1.1	1.6	0.7	0.2	0.3	0.4
Diaphragm/spermicide*	1.9	1.2	1.2	1.3	2.2	2.8
Periodic abstinence*	2.5	1.6	1.6	1.7	2.9	3.6

*Deaths are birth-related
**Deaths are method-related
Adapted from H.W. Ory, ref. #35.

In the above table, the risk of death from any birth control method is less than the risk of childbirth, except for oral contraceptive users over the age of 35 who smoke and pill users over the age of 40 even if they do not smoke. It can be seen in the table that for women aged 15 to 39, the risk of death was highest with pregnancy (7-26 deaths per 100,000 women, depending on age). Among pill users who do not smoke, the risk of death was always lower than that associated with pregnancy for any age group, although over the age of 40, the risk increases to 32 deaths per 100,000 women, compared to 28 associated with pregnancy at that age. However, for pill users who smoke and are over the age of 35, the estimated number of deaths exceeds those for other methods of birth control. If a woman is over the age of 40 and smokes, her estimated risk of death is four times higher (117/100,000 women) than the estimated risk associated with pregnancy (28/100,000 women) in that age group.

The suggestion that women over 40 who do not smoke should not take oral contraceptives is based on information from older, higher-dose pills. An Advisory Committee of the FDA discussed this issue in 1989 and recommended that the benefits of low-dose oral contraceptive use by healthy, non-smoking women over 40 years of age may outweigh the possible risks.

WARNING SIGNALS

If any of these adverse effects occur while you are taking oral contraceptives, call your doctor immediately:

- Sharp chest pain, coughing of blood, or sudden shortness of breath (indicating a possible clot in the lung)
- Pain in the calf (indicating a possible clot in the leg)
- Crushing chest pain or heaviness in the chest (indicating a possible heart attack)
- Sudden severe headache or vomiting, dizziness or fainting, disturbances of vision or speech, weakness, or numbness in an arm or leg (indicating a possible stroke)
- Sudden partial or complete loss of vision (indicating a possible clot in the eye)
- Breast lumps (indicating possible breast cancer or fibrocystic disease of the breast; ask your doctor or health care provider to show you how to examine your breasts)
- Severe pain or tenderness in the stomach area (indicating a possibly ruptured liver tumor)
- Difficulty in sleeping, weakness, lack of energy, fatigue, or change in mood (possibly indicating severe depression)
- Jaundice or a yellowing of the skin or eyeballs, accompanied frequently by fever, fatigue, loss of appetite, dark colored urine, or light colored bowel movements (indicating possible liver problems)

SIDE EFFECTS OF ORAL CONTRACEPTIVES

1. Vaginal Bleeding

Irregular vaginal bleeding or spotting may occur while you are taking the pills. Irregular bleeding may vary from slight staining between menstrual periods to breakthrough bleeding which is a flow much like a regular period. Irregular bleeding occurs most often during the first few months of oral contraceptive use, but may also occur after you have been taking the pill for some time. Such bleeding may be temporary and usually does not indicate any serious problems. It is important to continue taking your pills on schedule. If the bleeding occurs in more than one cycle or lasts for more than a few days, talk to your doctor or health care provider.

2. Contact Lenses

If you wear contact lenses and notice a change in vision or an inability to wear your lenses, contact your doctor or health care provider.

3. Fluid Retention

Oral contraceptives may cause edema (fluid retention) with swelling of the fingers or ankles and may raise your blood pressure. If you experience fluid retention, contact your doctor or health care provider.

4. Melasma

A spotty darkening of the skin is possible, particularly of the face, which may persist.

5. Other Side Effects

Other side effects may include nausea and vomiting, change in appetite, headache, nervousness, depression, dizziness, loss of scalp hair, rash, and vaginal infections.

If any of these side effects bother you, call your doctor or health care provider.

GENERAL PRECAUTIONS

1. Missed Periods and Use of Oral Contraceptives Before or During Early Pregnancy

There may be times when you may not menstruate regularly after you have completed taking a cycle of pills. If you have taken your pills regularly and miss one menstrual period, continue taking your pills for the next cycle but be sure to inform your health care provider before doing so. If you have not taken the pills daily as instructed and missed a menstrual period, you may be pregnant. If you missed two consecutive menstrual periods, you may be pregnant. Check with your health care provider immediately to determine whether you are pregnant. Do not continue to take oral contraceptives until you are sure you are not pregnant, but continue to use another method of contraception.

There is no conclusive evidence that oral contraceptive use is associated with an increase in birth defects, when taken inadvertently during early pregnancy. Previously, a few studies had reported that oral contraceptives might be associated with birth defects, but these findings have not been seen in more recent studies. Nevertheless, oral contraceptives or any other drugs should not be used during pregnancy unless clearly necessary and prescribed by your doctor. You should check with your doctor about risks to your unborn child of any medication taken during pregnancy.

2. While Breast Feeding

If you are breast feeding, consult your doctor before starting oral contraceptives. Some of the drug will be passed on to the child in the milk. A few adverse effects on the child have been reported, including yellowing of the skin (jaundice) and breast enlargement. In addition, combination oral contraceptives may decrease the amount and quality of your milk. If possible, do not use combination oral contraceptives while breast feeding. You should use another method of contraception since breast feeding provides only partial protection from becoming pregnant and this partial protection decreases significantly as you breast feed for longer periods of time. You should consider starting combination oral contraceptives only after you have weaned your child completely.

3. Laboratory Tests

If you are scheduled for any laboratory tests, tell your doctor you are taking birth control pills. Certain blood tests may be affected by birth control pills.

4. Drug Interactions

Certain drugs may interact with birth control pills to make them less effective in preventing pregnancy or cause an increase in breakthrough bleeding. Such drugs include rifampin, drugs used for epilepsy such as barbiturates (for

See reverse side for additional information.

HOW TO TAKE THE PILL

IMPORTANT POINTS TO REMEMBER

BEFORE YOU START TAKING YOUR PILLS:

1. BE SURE TO READ THESE DIRECTIONS:
Before you start taking your pills.

2. THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.
If you miss pills you could get pregnant. This includes starting the pack late. The more pills you miss, the more likely you are to get pregnant.

3. MANY WOMEN HAVE SPOTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE FIRST 1-3 PACKS OF PILLS. If you feel sick to your stomach, do not stop taking the pill. The problem will usually go away. If it doesn't go away, check with your doctor or clinic.

4. MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING, even when you make up these missed pills. On the days you take 2 pills to make up for missed pills, you could also feel a little sick to your stomach.

5. IF YOU HAVE VOMITING OR DIARRHEA, for any reason, or **IF YOU TAKE SOME MEDICINES,** including some antibiotics, your pills may not work as well. Use a back-up method (such as condoms, foam, or sponge) until you check with your doctor or clinic.

6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your doctor or clinic about how to make pill-taking easier or about using another method of birth control.

7. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your doctor or clinic.

BEFORE YOU START TAKING YOUR PILLS

1. DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL.
It is important to take it at about the same time every day.

2. LOOK AT YOUR PILL PACK TO SEE THAT IT HAS 28 PILLS:
The 28-pill pack has 21 "active" blue pills (with hormones) to take for 3 weeks. This is followed by 1 week of "reminder" teal pills (without hormones).

3. ALSO FIND:
1) where on the pack to start taking pills,
2) in what order to take the pills.

CHECK PICTURE OF PILL PACK AND ADDITIONAL INSTRUCTIONS FOR USING THIS PACKAGE IN THE BRIEF SUMMARY PATIENT PACKAGE INSERT.

4. BE SURE YOU HAVE READY AT ALL TIMES: ANOTHER KIND OF BIRTH CONTROL (such as condoms, foam, or sponge) to use as a back-up method in case you miss pills.

AN EXTRA, FULL PILL PACK.

WHEN TO START THE FIRST PACK OF PILLS

You have a choice of which day to start taking your first pack of pills. PREVIFEM™ Tablets are available in the blister pack tablet dispenser which is preset for a Sunday Start. Day 1 Start is also provided. Decide with your doctor or clinic which is the best day for you. Pick a time of day which will be easy to remember.

SUNDAY START:
Take the first "active" blue pill of the first pack on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the pack that same day.

Use another method of birth control as a back-up method if you have sex anytime from the Sunday you start your first pack until the next Sunday (7 days). Condoms, foam, or the sponge are good back-up methods of birth control.

DAY 1 START:
Take the first "active" blue pill of the first pack during the first 24 hours of your period.

You will not need to use a back-up method of birth control, since you are starting the pill at the beginning of your period.

WHAT TO DO DURING THE MONTH

1. TAKE ONE PILL AT THE SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY.
Do not skip pills even if you are spotting or bleeding between monthly periods or feel sick to your stomach (nausea).
Do not skip pills even if you do not have sex very often.

2. WHEN YOU FINISH A PACK OR SWITCH YOUR BRAND OF PILLS:
Start the next pack on the day after your last "reminder" pill.
Do not wait any days between packs.

WHAT TO DO IF YOU MISS PILLS

If you **MISS 1** blue "active" pill:
1. Take it as soon as you remember. Take the next pill at your regular time. This means you may take 2 pills in 1 day.
2. You do not need to use a back-up birth control method if you have sex.

If you **MISS 2** blue "active" pills in a row in **Week 1 OR Week 2** of your pack:
1. Take 2 pills on the day you remember and 2 pills the next day.
2. Then take 1 pill a day until you finish the pack.
3. You **MAY BECOME PREGNANT** if you have sex in the 7 days after you miss pills. You **MUST** use another birth control method (such as condoms, foam, or sponge) as a back-up method for those 7 days.

If you **MISS 2** blue "active" pills in a row in **THE 3RD Week:**
1. **If you are a Sunday Starter:**

anticonvulsants such as carbamazepine (Tegretol is one brand of this drug), phenytoin (his drug), phenylbutazone (Butazolidin is one brand) and possibly certain antibiotics. You ıl contraception when you take drugs which can make oral contraceptives less effective.

)iseases

ıll oral contraceptives) are intended to prevent pregnancy. Oral contraceptives do not pro- of HIV (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, ıepatitis B, and syphilis

HOW TO TAKE THE PILL

IMPORTANT POINTS TO REMEMBER

NG YOUR PILLS:

:SE DIRECTIONS:
ur pills.

what to do.

.KE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.
ł get pregnant. This includes starting the pack late. The more pills you miss, the more ant.

POTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE .S. If you feel sick to your stomach, do not stop taking the pill. The problem will usually way, check with your doctor or clinic.

.SO CAUSE SPOTTING OR LIGHT BLEEDING, even when you make up these missed pills.
ls to make up for missed pills, you could also feel a little sick to your stomach.

G OR DIARRHEA, for any reason, or **IF YOU TAKE SOME MEDICINES,** including some not work as well. Use a back-up method (such as condoms, foam, or sponge) until you clinic.

REMEMBERING TO TAKE THE PILL, talk to your doctor or clinic about how to make pill- ıg another method of birth control.

STIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your doc-

BEFORE YOU START TAKING YOUR PILLS

: DAY YOU WANT TO TAKE YOUR PILL.
about the same time every day.

ıCK TO SEE THAT IT HAS 28 PILLS:
active" blue pills (with hormones) to take for 3 weeks. This is followed by 1 week of ɔut hormones).

art taking pills,

e pills.

. PACK AND ADDITIONAL INSTRUCTIONS FOR USING THIS PACKAGE IN THE BRIEF ŁAGE INSERT.

:ADY AT ALL TIMES:
CONTROL (such as condoms, foam, or sponge) to use as a back-up method in case you

CK.

WHEN TO START THE FIRST PACK OF PILLS

h day to start taking your first pack of pills. PREVIFEM™ tablets are available in the blis- vhich is preset for a Sunday Start. Day 1 Start is also provided. Decide with your doctor day for you. Pick a time of day which will be easy to remember.

pill of the first pack on the Sunday after your period starts, even if you are still bleeding. unday, start the pack that same day.

th control as a back-up method if you have sex anytime from the Sunday you start your ınday (7 days). Condoms, foam, or the sponge are good back-up methods of birth con-

pill of the first pack during the first 24 hours of your period.

back-up method of birth control, since you are starting the pill at the beginning of your

WHAT TO DO DURING THE MONTH

: SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY.
ɔu are spotting or bleeding between monthly periods or feel sick to your stomach (nau-

ɔu do not have sex very often.

'ACK OR SWITCH YOUR BRAND OF PILLS:
day after your last "reminder" pill. Do not wait any days between packs.

WHAT TO DO IF YOU MISS PILLS

:" pill:

remember. Take the next pill at your regular time. This means you may take 2 pills in 1

a back-up birth control method if you have sex.

" pills in a row in **Week 1 OR Week 2** of your pack:

you remember and 2 pills the next day.

ntil you finish the pack.

3NANT if you have sex in the 7 days after you miss pills. You **MUST** use another birth con- oms, foam, or sponge) as a back-up method for those 7 days.

" pills in a row in **THE 3RD Week**:

ırter:
y until Sunday. On Sunday, **THROW OUT** the rest of the pack and start a new pack of pills

:
ıe pill pack and start a new pack that same day.

period this month but this is expected. However, if you miss your period 2 months in a nic because you might be pregnant.

3NANT if you have sex in the 7 days after you miss pills. You **MUST** use another birth con- oms, foam, or sponge) as a back-up method for those 7 days.

ɔlue "active" pills in a row (during the first 3 weeks):

ırter:
y until Sunday. On Sunday, **THROW OUT** the rest of the pack and start a new pack of pills

:
ıe pill pack and start a new pack that same day.

period this month but this is expected. However, if you miss your period 2 months in a nic because you might be pregnant.

3NANT if you have sex in the 7 days after you miss pills. You **MUST** use another birth con- oms, foam, or sponge) as a back-up method for those 7 days.

: ON 28-DAY PACKS:
teal "reminder" pills in Week 4:
ɔu missed.

y until the pack is empty.
p method.

LL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED:
anytime you have sex.
VE" PILL EACH DAY until you can reach your doctor or clinic.

3. YOU MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You **MUST** use another birth control method (such as condoms, foam, or sponge) as a back-up method for those 7 days.

If you **MISS 3 OR MORE** blue "active" pills in a row (during the first 3 weeks):

1. **If you are a Sunday Starter:**
Keep taking 1 pill every day until Sunday. On Sunday, **THROW OUT** the rest of the pack and start a new pack of pills that same day.

If you are a Day 1 Starter:
THROW OUT the rest of the pill pack and start a new pack that same day.

2. You may not have your period this month but this is expected. However, if you miss your period 2 months in a row, call your doctor or clinic because you might be pregnant.

3. You **MAY BECOME PREGNANT** if you have sex in the 7 days after you miss pills. You **MUST** use another birth control method (such as condoms, foam, or sponge) as a back-up method for those 7 days.

A REMINDER FOR THOSE ON 28-DAY PACKS:

If you forget any of the 7 teal "reminder" pills in Week 4:

THROW AWAY the pills you missed.

Keep taking 1 pill each day until the pack is empty.

You do not need a back-up method.

FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED:

Use a **BACK-UP METHOD** anytime you have sex.

KEEP TAKING ONE "ACTIVE" PILL EACH DAY until you can reach your doctor or clinic.

Instructions for Using Your Blister Pack Tablet Dispenser

PLEASE READ ME!

✎

☐ Sunday Start

Or

☐ Day 1 Start

There are two ways to start taking birth control pills, Sunday Start or Day 1 Start. Your health care provider will tell you which to use.

Save these instructions.

1

If this is the first time you are taking birth controls pills, or if you have not taken birth control pills for 10 days or more, your first step is to **wait until the first day you get your menstrual period.** Then, follow these instructions for either Sunday Start or Day 1 Start.

2

☐ Sunday Start

☐ Day 1 Start

When you get your period:

- You will use a **Sunday Start** if your doctor told you to take your first pill on a Sunday. Take pill "1" on the Sunday after your period starts. If your period starts on a Sunday, take pill "1" that day.
- You will use a **Day 1 Start** if your doctor told you to take pill "1" on the first day of your period.

3

Sunday Start: Discard calendar label.

Day 1 Start: Place label strip, which corresponds to the first day of your period (if your period starts on Tuesday (TUE), start the labels with TUE beginning first.

4

Remove pill "1" by pushing down on the pill. The pill will come out through the foil in the back.

5

Swallow the pill. You will take one pill each day, if you use a Sunday Start and you are taking the pill for the **FIRST TIME, YOU MUST USE A BACK-UP METHOD OF BIRTH CONTROL FOR THE FIRST 7 DAYS.** If you use a Day 1 Start, you are protected from becoming pregnant as soon as you take your first pill.

6

Wait 24 hours to take your next pill. To take pill "2", proceed to next pill in blister pack. Continue to take one pill each day until all the pills have been taken.

7

Take your pill at the same time every day. It is important to take the correct pill each day and not miss any pills. To help you remember, take your pill at the same time as another daily activity, like turning off your alarm clock or brushing your teeth.

8

When your pack is empty,

- You will start a new pack on the day after pill "28".

9

THE FIRST PILL IN EVERY PACK WILL ALWAYS BE TAKEN ON THE SAME DAY OF THE WEEK, NO MATTER WHEN YOUR NEXT PERIOD STARTS.

If you miss one pill... take it as soon as you remember. Take the next pill at your regular time. This means you may take two pills in one day. You will not need a back-up method of birth control if you have sex.

If you miss two or more pills in a row... YOU MAY BECOME

a. If you miss two pills in a row of pills in Week 1 or Week 2 of your pack:
Take two pills as soon as you remember and two pills the next day, then keep taking one pill each day as usual.

b. If you miss two pills in **Week 2** or **Week 3** or if you miss two pills in a row in **Week 3** or if you miss three or more pills in a row during the first 3 weeks:
Keep taking one pill each day until Sunday.
On Sunday, ***THROW OUT*** *the rest of the pills and start a new pack.*

☐ **Day 1 Start** ✎

a. If you miss two pills in a row of pills in Week 1 or Week 2 of your pack:
Take two pills as soon as you remember and two pills the next day, then keep taking one pill each as usual.

b. If you miss two pills in Week 2 or Week 3 or if you miss two pills in a row **in Week 3** or if you miss three or more pills in a row during the first 3 weeks:
THROW OUT *the rest of the pills and start a new pack that day.*

If you miss pills in Week 4...
Remember that pills **in Week 4** are "reminder" pills and do not contain active ingredients.

- If you miss any pills in Week 4, you will still be protected:
Throw away the missed pills and keep taking one pill each day until you finish the pack. Start a new pack on the day after the last pill.

Side Effects:
Some side effects are normal and will go away after the first 1, 2 or 3 months as your body gets used to the pill. For more information on side effects see the Brief Summary, the Detailed Patient Information Labeling that comes with your pills, or ask your health care provider or pharmacist.

Manufactured by:
Andrx Pharmaceuticals, Inc.
Ft. Lauderdale, FL 33314

Rev. date: 10/03 7309

The incidence of pill failure resulting in pregnancy is approximately one percent (1%) (one pregnancy per 100 women per year) if taken every day as directed, but more typical failure rates are 3%. If failure does occur, the risk to the fetus is minimal.

PREGNANCY AFTER STOPPING THE PILL
There may be some delay in becoming pregnant after you stop using oral contraceptives, especially if you had irregular menstrual cycles before you used oral contraceptives. It may be advisable to postpone conception until you begin menstruating regularly once you have stopped taking the pill and desire pregnancy.

There does not appear to be any increase in birth defects in newborn babies when pregnancy occurs soon after stopping the pill.

OVERDOSAGE
Serious ill effects have not been reported following ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea and withdrawal bleeding in females. In case of overdosage, contact your health care provider or pharmacist.

OTHER INFORMATION
Your health care provider will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be delayed to another time if you request it and the health care provider believes that it is a good medical practice to postpone it. You should be reexamined at least once a year. Be sure to inform your health care provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your health care provider, because this is a time to determine if there are early signs of side effects of oral contraceptive use.

Do not use the drug for any condition other than the one for which it was prescribed. This drug has been prescribed specifically for you; do not give it to others who may want birth control pills.

HEALTH BENEFITS FROM ORAL CONTRACEPTIVES
In addition to preventing pregnancy, use of combination oral contraceptives may provide certain benefits.

They are:

- menstrual cycles may become more regular
- blood flow during menstruation may be lighter and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.
- pain or other symptoms during menstruation may be encountered less frequently
- ectopic (tubal) pregnancy may occur less frequently
- noncancerous cysts or lumps in the breast may occur less frequently
- acute pelvic inflammatory disease may occur less frequently
- oral contraceptive use may provide some protection against developing two forms of cancer: cancer of the ovaries and cancer of the lining of the uterus.

If you want more information about birth control pills, ask your doctor/health care provider or pharmacist. They have a more technical leaflet called the Professional Labeling, which you may wish to read. The professional labeling is also published in a book entitled *Physicians' Desk Reference*, available in many book stores and public libraries.

Manufactured by:
Andrx Pharmaceuticals, Inc.
Ft. Lauderdale, FL 33314

Rev. date: 10/03 7308

76-334

Previfem™
(norgestimate and ethinyl estradiol)

Contains: 6 Blister Packs,
28 Tablets Each and
6 Label Strips

6 Blister Packs 28 Day Regimen

NDC 62037-751-28

Previfem™
(norgestimate and ethinyl estradiol)

Each blue tablet contains 0.25 mg norgestimate and 0.035 mg ethinyl estradiol. Each teal tablet contains inert ingredients.

Rx Only

Store at 25° C (77° F) [see USP Controlled Room Temperature.]; excursions permitted to 15° - 30° C (59° - 86° F).

Manufactured by:
Andrx Pharmaceuticals, Inc.
Ft. Lauderdale, FL 33314
www.andrx.com

Rev. date 09/03 7314

Lot:
Exp:

7314

JAN 0 9 2004

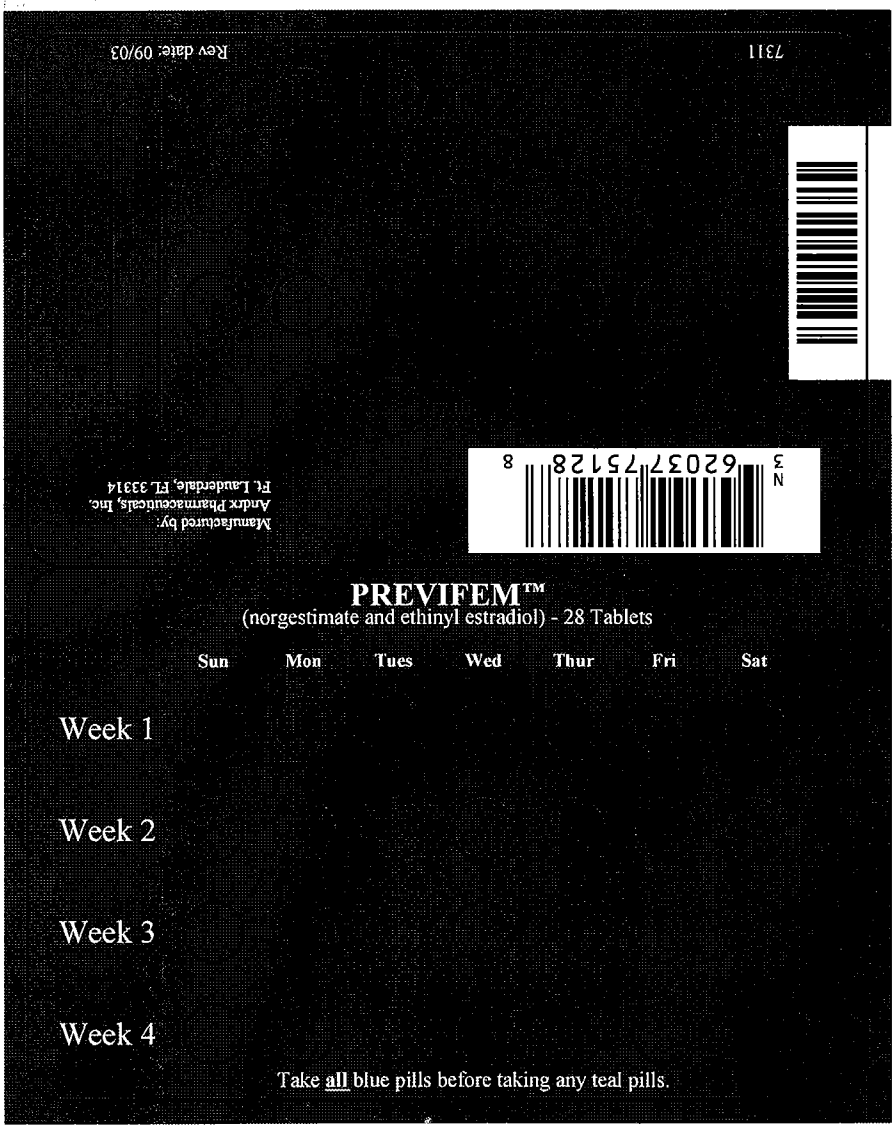
Each blue tablet contains 0.25 mg norgestimate and 0.035 mg ethinyl estrad
Each teal tablet contains inert ingredients.

Dosage: One tablet daily as prescribed. See package insert.

Important: Each sleeve contains a combination Brief Summary Patient Pack
Insert and Detailed Patient Labeling. This should be included with each
package dispensed to the patient.

N3 62037 75128

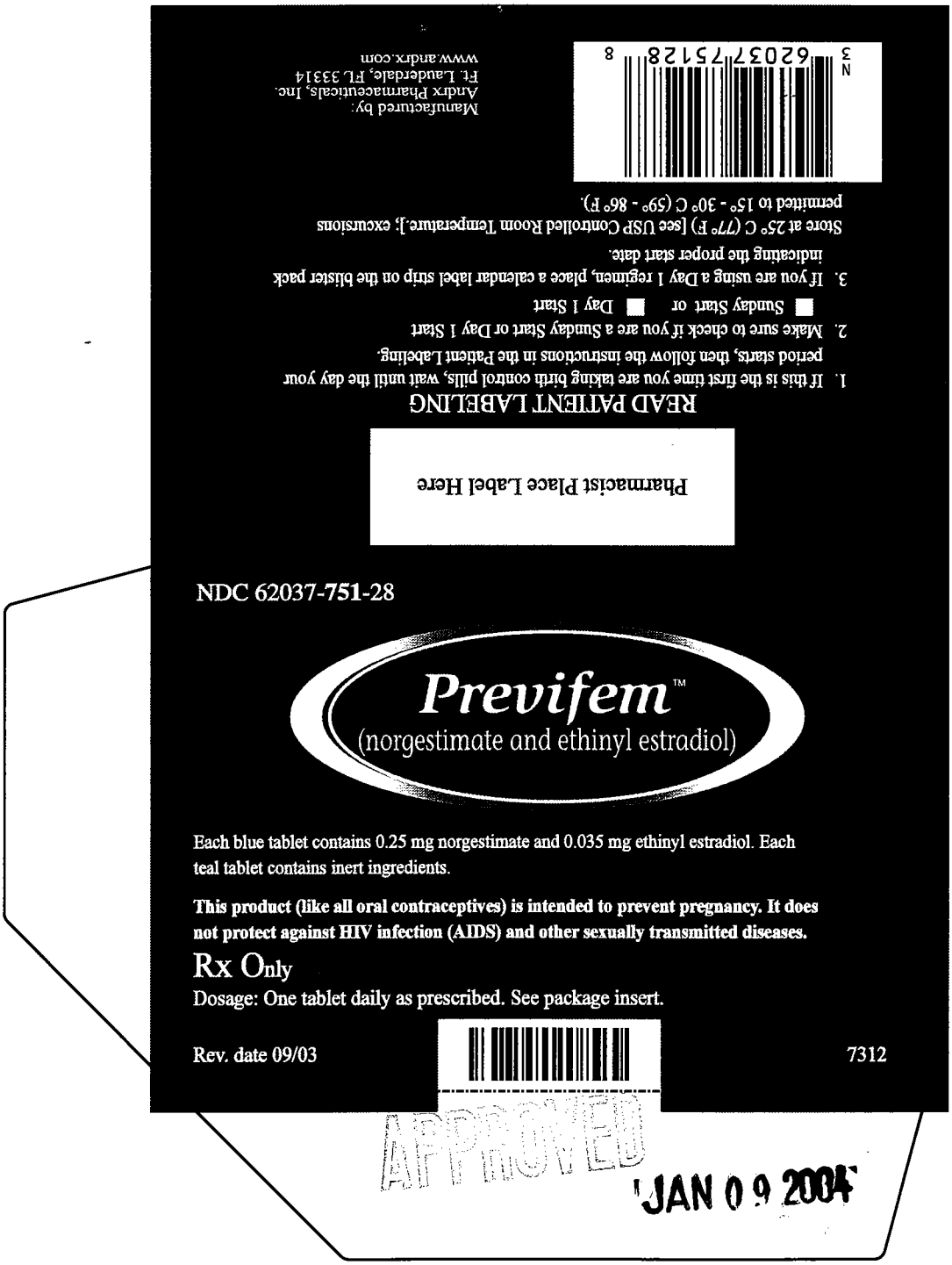
ANDA #76-334
PREVIFEM™
(norgestimate [0.25 mg]
and ethinyl estradiol [0.035 mg])Tablets
FINAL PRINTED LABELING



76-334

76-334

ANDA #76-334
PREVIFEM™
(norgestimate [0.25 mg]
and ethinyl estradiol [0.035 mg])Tablets
FINAL PRINTED LABELING



HOW TO USE THIS BLISTER PACK

APPROVED JAN 09 2004

MON	TUE	WED	THU	FRI	SAT	SUN
TUE	WED	THU	FRI	SAT	SUN	MON
WED	THU	FRI	SAT	SUN	MON	TUE
THU	FRI	SAT	SUN	MON	TUE	WED
FRI	SAT	SUN	MON	TUE	WED	THU
SAT	SUN	MON	TUE	WED	THU	FRI

FOR USE WITH DAY 1 START REGIMEN ONLY

NOTICE

Oral contraceptives are intended to prevent pregnancy. They do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases.

USE OF CALENDER LABEL (On the other side)

- **If Sunday start, discard calendar label.**
- **If DAY 1 START:**
  1. **Find the label strip (see other side) that starts with the day of the week your period begins.**
  2. **Peel that label strip and place it on the top of the blister pack across the area where each day of the week is printed.**
  3. **Firmly press label on blister pack.**

Rev date: 03/03

7313

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-334

LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-334

Date of Submission: December 27, 2001 (Original) and July 17, 2002 (Amendment)

Applicant's Name: Andrx Pharmaceuticals, Inc.

Established Name: Norgestimate and Ethinyl Estradiol Tablets, 0.25 mg/0.035 mg (28 day regimen)

Proprietary Name: Previfem™ Tablets

2.1

Labeling Deficiencies:

1. **GENERAL COMMENT:**

We have completed our nomenclature review and have no objection to the use of the proprietary name "Previfem™" for your drug product.

2. **CONTAINER** (Blister Pack Tablet Dispenser – 28 Day):
3. **CALENDAR LABEL STRIP** (To be affixed to the blister pack):
4. **CARDBOARD SLEEVE** (To contain the blister pack and calendar label strip):
5. **CARTON** (Box of 6 blister packs):

Please refer to pages "0032 - 0036" of the attached mocked-up copy of your draft labeling for all of the requested labeling revisions.

6. **PROFESSIONAL PACKAGE INSERT**:

Please refer to pages "0039-43, 0045-48, 0051-53, 0056-58, 0065-66, 0070, 0073-75, and 0077" of the attached mocked-up copy of your draft insert labeling for all of the requested labeling revisions:

7. **BRIEF SUMMARY PATIENT PACKAGE INSERT**:

Please refer to pages "0081, 0083, and 0087-90" of the attached mocked-up copy of your draft labeling for all of the requested labeling revisions:

8. **DETAILED PATIENT LABELING INSERT**:

Please refer to page "0092" of the attached mocked-up copy of your draft labeling for all of the requested labeling revisions:

Please revise your labels and labeling, as instructed above, and submit in final print.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Attachment: Mocked-up copy of the firm's draft labeling.

_34_ pages of draft labeling have been removed from this portion of the document.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's Established Name	Yes	No	N/A
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured.		x	
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?	x		
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	x		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?		x	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified? **The proposed name "Previfem™" was found acceptable by DMETS on October 8, 2002 (Consult #02-0159)**	x		
PACKAGING -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. [see FTR]		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	X		
Are there any other safety concerns?		X	
LABELING			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?		X	

Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (p. #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?	X		
Inactive Ingredients: (FTR: List p. # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?	X		
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?[see FTR]		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			

Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. **NONE.**		X	

FOR THE RECORD:

1. MODEL LABELING

   This review was based on the labeling for Ortho-Cyclen® Tablets (28 Day Regimen) by R.W. Johnson (NDA 19-653/S-025; revised January 2000 and approved June 5, 2000; and S-027, revised April 2000 and approved January 16, 2001 (Detailed Patient and Brief Summary Patient Inserts only).

2. PATENTS/EXCLUSIVITIES

   Patent Data – NDA 19-653

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

   Exclusivity Data– NDA 19-653

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

   The firm's statements are correct. [Vol. A1.1 pg. 0006-7.]

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

   Andrx Pharmaceuticals, Inc.
   4955 Orange Drive
   Ft. Lauderdale, FL 33314 [Vol. A1.2 pg. 0372.]

4. CONTAINER/CLOSURE

   Blister Film: [redacted] clear transparent plastic film.
   Blister Backing: [redacted] push thru Aluminum Foil with [redacted]

   [Vol. A1.3 pg. 0687-698.]

5. INACTIVE INGREDIENTS

   The description of the inactive ingredients in the insert labeling is NOT accurate according to the composition statement. I have asked the firm to revise. [Vol. A1.1 pg. 0258.]

6. PACKAGING CONFIGURATIONS

   RLD: Cartons of 6 x 21-Day and 6 x 28-Day Dialpak® Tablet Dispensers.
   1 x 21-Day and 1 x 28-Day Veridate® Tablet Dispensers (unfilled) for clinic use.
   ANDA: Cartons of 6 x 28-Day Blister Pack Tablet Dispenser with cardboard sleeve.
   [Vol. A1.3 pg. 0698.]

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: None.
RLD: None.
ANDA: None. (However I have asked the firm to include their storage temp. statement on their labeling.)
[Vol. A1.1 pg. 0152.]

8. DISPENSING STATEMENTS COMPARISON

USP: None
RLD: **IMPORTANT:** Each carton contains Detailed Patient Labeling and each DIALPAK® Tablet Dispenser contains the Brief Patient Labeling. Both should be included with each package dispensed to the patient.
ANDA:**IMPORTANT:** Each sleeve contains a combination Brief Summary Patient Package Insert and Detailed Patient Labeling. This should be included with each package dispensed to the patient.
[Vol. A1.1 pg. 0115.]

9. TABLET IMPRINT

The tablet imprintings have been accurately described in the HOW SUPPLIED section of the Insert according to the firm's Finished Product Specifications:

"active" tablet: "blue, round, film coated, tablet with Andrx logo on one side and **748** on the other side."
placebo tablet: "teal, round, film coated, tablet with Andrx logo on one side and **743** on the other side."

I have asked the firm to include "unscored" in the description of the active tablet.
[Vol. A1.3 pg. 0719 and 0733.]

10. BIOAVAILABILITY/BIOEQUIVALENCE:

The Division of Bioequivalence concluded on September 16, 2002, that the firm's bioequivalency data were acceptable.

11. NOMENCLATURE:

The firm proposed the proprietary name "Previfem™ " for their product. DMETS concluded on October 8, 2002, that "Previfem" was an acceptable name for this drug product (Consult #02-0159).

Date of Review: 3/3/03 Dates of Submission: 12/27/01 and 7/17/02

Primary Reviewer: Debra Catterson Date:

Debra M. Catterson 3/4/03

Team Leader: John Grace Date:

John J Grace 3/5/2003

---

cc:

ANDA: 76-334
DUP/DIVISION FILE
HFD-613/DCatterson/JGrace (no cc)
v:\firmsam\andrx\ltrs&rev\76334NA1.L.doc
Review