

NDA 20-262/S-032

DEC 10 1999

Bristol-Myers Squibb Company
5 Research Parkway
Wallingford, CT 06492

Attention: Susan H. Behling, Director
Global Oncology Strategic Unit
Regulatory Sciences

Dear Ms. Behling:

Please refer to your supplemental new drug application dated February 5, 1999, received February 8, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TAXOL (paclitaxel) Injection.

We acknowledge receipt of your submissions dated July 12, and September 14, 1999.

This supplemental new drug application provides a patient information leaflet.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon patient information labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

In addition, please revise the approved package insert dated October 25, 1999 to include the following statement at the end of the **PRECAUTIONS** section:

Information for Patients: (See Patient Information Leaflet.)

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the patient package insert) and the October 25, 1999 approved package insert with the revision requested above.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-262/S-032." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we

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request that you submit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Leslie Vaccari, Project Manager, at (301) 594-5784. Sincerely.

Richard Pazdur, M.D.
Director
Division of Oncologic Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Patient Information

TAXOL® Injection

(generic name = paclitaxel)

What is TAXOL?

TAXOL is a prescription cancer medicine, it is injected into a vein and it is used to treat different types of tumors. The tumors include advanced ovary and breast cancer. The tumors also include certain lung cancers (non-small cell) in people who cannot have surgery or radiation therapy. TAXOL may also be used to treat AIDS-related Kaposi's sarcoma.

What is cancer?

Under normal conditions, the cells in your body divide and grow in an orderly, controlled way. Cell division and growth are necessary for the human body to perform its functions and to repair itself, when necessary. Cancer cells are different from normal cells because they are not able to control their own growth. The reasons for this abnormal growth are not yet fully understood.

A tumor is a mass of unhealthy cells that are dividing and growing fast and in an uncontrolled way. When a tumor invades surrounding healthy body tissue it is known as a malignant tumor. A malignant tumor can spread (metastasize) from its original site to other parts of the body if not found and treated early.

How does TAXOL work?

TAXOL is a type of medical treatment called chemotherapy. The purpose of chemotherapy is to kill cancer cells or prevent their growth.

All cells, whether they are healthy cells or cancer cells, go through several stages of growth. During one of the stages, the cell starts to divide. TAXOL may stop the cells from dividing and growing, so they eventually die. In addition, normal cells may also be affected by TAXOL causing some of the side effects. (See **What are the possible side effects of TAXOL?** below.)

Who should not take TAXOL?

Patients who have a history of hypersensitivity (allergic reactions) to TAXOL or other drugs containing Cremophor® EL* (polyoxyethylated castor oil), like cyclosporine or teniposide, should not be given TAXOL. In addition, TAXOL should not be given to patients with dangerously low white blood cell counts.

How is TAXOL given?

TAXOL is injected into a vein (intravenous (IV) infusion). Before you are given TAXOL, you will have to take certain medicines (premedications) to prevent or reduce the chance you will have a serious allergic reaction. Such reactions have occurred in a small number of patients while receiving TAXOL and have been rarely fatal. (See **What are the possible side effects of TAXOL?** below.)

What are the possible side effects of TAXOL?

Most patients taking TAXOL will experience side effects, although it is not always possible to tell whether such effects are caused by TAXOL, another medicine they may be taking, or the cancer itself. Important side effects are described below; however some patients may experience other side effects that are less common. Report any unusual symptoms to your doctor.

Important side effects observed in studies of patients taking TAXOL were as follows:

- allergic reactions.* Allergic reactions can vary in degrees of severity. They may cause death in rare cases. When a severe allergic reaction develops, it usually occurs at the time the medicine is entering the body (during TAXOL infusion). Allergic reactions may cause trouble breathing, very low blood pressure, sudden swelling, and/or hives or rash. The likelihood of a serious allergic reaction is lowered by the use of several kinds of medicines that are given to you before the TAXOL infusion.
- heart and blood vessel (cardiovascular) effects.* TAXOL may cause a drop in heart rate (bradycardia) and low blood pressure (hypotension). The patient usually does not notice these changes. These changes usually do not require treatment. Your heart function, including blood pressure and pulse, will be monitored while you are receiving the medicine. You should notify your doctor if you have a history of heart disease.
- infections due to low white blood cell count.* Among the body's defenses against bacterial infections are white blood cells. Between your TAXOL treatment cycles, you will often have blood tests to check your white blood cell counts.

TAXOL usually causes a brief drop in white blood cells. *If you have a fever (temperature above 100.4° F) or other sign of infection, tell your doctor right away. Sometimes serious infections develop that require treatment in the hospital with antibiotics. Serious illness or death could result if such infections are not treated when white blood cell counts are low.*

- hair loss.* Complete hair loss, or alopecia, almost always occurs with TAXOL. This usually involves the loss of eye-brows, eyelashes, and pubic hair, as well as scalp hair. It can occur suddenly after treatment has begun, but usually happens 14 to 21 days after treatment. *Hair generally grows back after you've finished your TAXOL treatment.*
 - joint and muscle pain.* You may get joint and muscle pain a few days after your TAXOL treatment. These symptoms usually disappear in a few days. Although pain medicine may not be necessary, tell your doctor if you are uncomfortable.
 - irritation at the injection site.* TAXOL sometimes causes irritation at the site where it enters the vein. Reactions may include discomfort, redness, swelling, inflammation (of the surrounding skin or of the vein itself), and ulceration (open sores). These reactions are usually caused by the IV (intravenous) fluid leaking into the surrounding area. *If you notice anything unusual at the site of the injection (needle), either during or after treatment, tell your doctor right away.*
 - low red blood cell count.* Red blood cells deliver oxygen to tissues throughout all parts of the body and take carbon dioxide from the tissues by using a protein called hemoglobin. A lowering of the volume of red blood cells may occur following TAXOL treatment causing anemia. Some patients may need a blood transfusion to treat the anemia. Patients can feel tired, tire easily, appear pale, and become short of breath. Contact your doctor if you experience any of these symptoms following TAXOL treatment.
 - mouth or lip sores (mucositis).* Some patients develop redness and/or sores in the mouth or on the lips. These symptoms might occur a few days after the TAXOL treatment and usually decrease or disappear within one week. Talk with your doctor about proper mouth care and other ways to prevent or reduce your chances of developing mucositis.
 - numbness, tingling, or burning in the hands and/or feet (neuropathy).* These symptoms occur often with TAXOL and usually get better or go away without medication within several months of completing treatment. However, if you are uncomfortable, tell your doctor so that he/she can decide the best approach for relief of your symptoms.
 - stomach upset and diarrhea.* Some patients experience nausea, vomiting, and/or diarrhea following TAXOL use. If you experience nausea or stomach upset, tell your doctor. Diarrhea will usually disappear without treatment; however, *if you experience severe abdominal or stomach area pain and/or severe diarrhea, tell your doctor right away.*
- Talk with your doctor or other healthcare professional to discuss ways to prevent or reduce some of these side effects. Because this leaflet does not include all possible side effects that can occur with TAXOL, it is important to talk with your doctor about other possible side effects.

Can I take TAXOL if I am pregnant or nursing a baby?

TAXOL could harm the fetus when given to a pregnant woman. Women should avoid becoming pregnant while they are undergoing treatment with TAXOL. Tell your doctor if you become pregnant or plan to become pregnant while taking TAXOL. Because studies have shown TAXOL to be present in the breast milk of animals receiving the drug. It may be present in human breast milk as well. Therefore, nursing a baby while taking TAXOL is NOT recommended.

This medicine was prescribed for your particular condition. This summary does not include everything there is to know about TAXOL. Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. If you have questions or concerns, or want more information about TAXOL, your doctor or pharmacist have the complete prescribing information upon which this guide is based. You may want to read it and discuss it with your doctor. Remember, no written summary can replace careful discussion with your doctor.



*Cremophor® EL is the registered trademark of BASF Aktiengesellschaft.
Cremophor® EL is further purified by a Bristol-Myers Squibb Company proprietary process before use.

This Patient Information Leaflet has been approved by the
U.S. Food and Drug Administration.

