018554_S022

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-554/S-022

APPROVAL LETTER

NDA 18-554/S-022

Schering Corporation
Attention: Mary Jane Nehring
Senior Director, Marketed Products
Support and Training, Worldwide Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, NJ 07033

30 MAR 2001

Dear Ms. Nehring:

Please refer to your supplemental new drug application dated March 5, 2001, received March6, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Eulexin® (flutamide) Capsules, USP.

This "Changes Being Effected" supplemental new drug application provides for the following revisions to the Patient Information Sheet in the **Who should not take the Eulexin product?** section (to make consistent with the package insert revisions submitted on March 5, 2001), and the **Where can I get further support?** section:

Who should not take EULEXIN product?

> "You should not take EULEXIN Capsules if you have liver problems or if you are allergic to it. EULEXIN Capsules are for use **only** in men, therefore ~~W~~women should not take EULEXIN Capsules."

Where can I get further support?

> "Patients taking EULEXIN Capsules have access to Schering's Commitment To Care[SM], which can help you find financial reimbursement assistance for your EULEXIN therapy. The following services are available (1-800-521-~~7517~~7157)
>
> - research into reimbursement options
> - advice on how to obtain reimbursement assistance
> - support through Schering's Indigent Patient program
> - access to flexible payment programs
> - ~~counseling from registered pharmacists~~
>
> Please ask your doctor about any questions concerning prostate cancer or EULEXIN Therapy, or you can also ask for a more detailed leaflet that is written for healthcare professionals. ~~Also, visit Schering's prostate cancer web site at www.prostate-cancer.com for more information.~~"

We have completed the review of this supplemental application 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 labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (Patient Information Sheet submitted March 6, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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 18-554/S-022." 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 Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, 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, call Jeanine Best, M.S.N., R.N., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Susan Allen, M.D., M.P.H.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

EULEXIN® (flutamide) Capsules

Important information for patients taking EULEXIN® (brand of flutamide) capsules.

Read this information carefully each time your prescription is refilled because there may be new information available. This summary does not tell you everything you need to know about EULEXIN therapy.Your doctor is the best source of information about your treatment. Ask your doctor about questions you have.

What is EULEXIN therapy?

EULEXIN, in combination with other therapies, is a treatment option for men with some types of prostate cancer

Prostate cancer results from the abnormal growth of prostate cells. Medical scientists do not know exacdy what causes the abnormal cells, but age. environment, and genetics are important factors. Male hormones ("androgens") cause the cancer to grow. The cancer growth can be slowed down by blocking the effect of androgens

The EULEXIN product is used together with an injection called "LH-RH agonist", as a combined treatment called "total androgen blockade". The goal of this treatment is to reduce androgen levels and to block the effect of androgen on the tumor.The LH-RH agonist reduces androgen levels. EULEXIN therapy blocks the effect of androgen on the tumor.

Who should not take the EULEXIN product?

You should not take EULEXIN Capsules if you have liver problems or if you are allergic to it. EULEXIN Capsules are for use **only** in men, therefore women should not take EULEXIN Capsules.

Are there important risks I should know about EULEXIN therapy?

Some men taking the EULEXIN product had liver injury and needed to be hospitalized. In rare cases, men died because of liver failure while they were taking EULEXIN. In about half of these cases, the liver failure occurred in the first 3 months that they were taking EULEXIN.

Because the EULEXIN product may cause liver failure, **it is very important that you have all blood tests recommended by your doctor.** These tests help identify whether you are having liver problems. A recommended schedule for these blood tests is:

- before starting EULEXIN treatment.
- every month for the first 4 months of therapy.
- periodically after the first 4 months.

In addition, you should call your doctor right away if you have any of the following signs or symptoms:

- loss of appetite.
- nausea and vomiting.
- stomach or abdominal pain.
- fatigue (feeling extremely tired).
- flu-like symptoms (muscle aches, soreness).
- brown urine.
- jaundice (yellowing of the skin or whites of the eyes).

These may be signs of liver failure.

How should I take EULEXIN capsules?

Take your EULEXIN capsules as your doctor has prescribed. The usual dosing is 2 capsules every 8 hours.

Your doctor will determine whether EULEXIN therapy is right for you based on many different factors. These include how large your tumor is, how far it has spread and your physical condition. In addition to EULEXIN, you may be getting other treatments, including regular injections of LH-RH agonist or radiation therapy. Do not stop or interrupt any treatment without consulting your healthcare professional.

If you miss a dose of EULEXIN capsules, simply continue therapy with your next scheduled dose. Do not try to make up for it by taking extra capsules

Can I take other medicines?

If you are taking any other medicines, especially warfarin (a blood-thinning drug), tell your doctor before beginning EULEXIN therapy.

What are the other possible side effects of taking EULEXIN capsules?

In a medical study, when EULEXIN was taken together with an LH-RH agonist, the most common side effects were hot flashes, loss of sex drive (libido) and impotence. In addition, some men had diarrhea, nausea or vomiting, and breast enlargement

In another medical study, when the EULEXIN product was taken together with goserelin acetate (an LH-RH agonist) and radiation therapy, the side effects of EULEXIN were about the same as when radiation therapy was given alone. These included hot flashes, diarrhea, nausea and skin rash.

What can I do if I get diarrhea?

If you experience moderate diarrhea due to EULEXIN capsules. the following advice may help:

- drink plenty of fluids.
  reduce your intake of dairy products (for example, milk, cheese, yogurt).
- increase your intake of whole grains. fruits, and vegetables.
- stop laxative use.
- take non-prescription anti-diarrheal medicines.

If your diarrhea continues or it becomes severe, contact your doctor right away.

Are there any other lab tests my doctor will be performing?

Your doctor may perform other regular tests (such as the PSA blood test) to ensure that your body is responding to treatment. Ask your doctor if you have any questions about how your EULEXIN therapy is being monitored.

Where can I get further support?

Patients taking EULEXIN capsules have access to Schering's COMMITMENT TO CARE™. which can help you find financial reimbursement for your EULEXIN therapy.The following services are available (1-800-521-7157):

- research into reimbursement options.
- advice on how to obtain reimbursement.
- support through Schering's Indigent Patient program.
- access to flexible payment programs.

Please ask your doctor about any questions concerning prostate cancer or EULEXIN therapy, or you can also ask for a more detailed leaflet that is written for healthcare professionals.

Schering ONCOLOGY BIOTECH

Eulexin flutamide

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-554/S-022

ADMINISTRATIVE DOCUMENTS

Division of Reproductive and Urologic Drug Products

Regulatory Project Manager Label Review

Application Number: NDA 18-554/S-022 Eulexin® (flutamide) Capsules, USP

Sponsor: Schering Corporation

Material Reviewed:

- Patient Information Sheet

Submission Date: March 6, 2001

Receipt Date: March 7, 2001

Background and Summary Description:
The sponsor submitted this "Special Supplement-Changes Being Effected" (CBE) to revise the Patient Information Sheet to make consistent with the CBE submission March 5, 2001 for the Package Insert (revision to the **WARNINGS** section – **Use in Women** to strengthen and further clarify the existing information), and to make corrections to the Commitment To Care℠ information.

Review:

The **Who should not take EULEXIN product?** section was revised as follows:

Who should not take EULEXIN product?

> "You should not take EULEXIN Capsules if you have liver problems or if you are allergic to it. EULEXIN Capsules are for use **only** in men, therefore ~~W~~women should not take EULEXIN Capsules."

The sponsor made the following revisions to the **Where can I get further support?** section:

Where can I get further support?

> "Patients taking EULEXIN Capsules have access to Schering's Commitment To Care℠, which can help you find financial reimbursement assistance for your EULEXIN therapy. The following services are available (1-800-521-~~7517~~7157)
>
> - research into reimbursement options
> - advice on how to obtain reimbursement assistance
> - support through Schering's Indigent Patient program
> - access to flexible payment programs
> - ~~counseling from registered pharmacists~~
>
> Please ask your doctor about any questions concerning prostate cancer or EULEXIN Therapy, or you can also ask for a more detailed leaflet that is written for healthcare professionals. ~~Also, visit Schering's prostate cancer web site at www.prostate-cancer.com for more information.~~"

The sponsor deleted that bullet stating "counseling from registered pharmacists" because this feature is not part of the reimbursement program offered through Commitment To Care[SM]. The sponsor also deleted the reference to their prostate cancer web site because the site is no longer active and will not be reinstated at this time.

Conclusions:
A sponsor may submit a CBE supplement to make changes to the labeling to "add or strengthen a contraindication, warning, precaution or adverse reaction" per CFR §314.70(2)(I). The revisions made to the **Where can I get further support?** section are acceptable because statements that were deleted were not approval conditions. An Approval Letter should be issued for NDA 18-554/S-022.

Jeanine A. Best, M.S.N., R.N.
Regulatory Project Manager

Concurrence:

Terri Rumble, B.S.N.
Chief, Project Management Staff

Mark Hirsch, M.D.
Urology Team Leader

Susan Allen, M.D., M.P.H.
Director

cc:
Orig. NDA 18-554
HFD-580/Div File
HFD-580/Best
Concurrence:Rumble,03.22.01/Hirsch,03.22.01/Allen,03.23.01
Drafted: JAB/March 22, 2001/N18554S22Labrev.doc
Final: JAB/March 23, 2001
REGULATORY MANAGER REVIEW

/s/

Jeanine Best
3/23/01 12:48:54 PM
CSO

Terri F. Rumble
3/23/01 02:26:08 PM
CSO

Mark S. Hirsch
3/27/01 02:07:27 PM
MEDICAL OFFICER

Susan Allen
3/30/01 04:21:29 PM
MEDICAL OFFICER

NDA 18-554/S-022

CBE-0 SUPPLEMENT

Schering Corporation
Attention: Mary Jane Nehring
Senior Director, Marketed Products
2000 Galloping Road
Kenilworth, NJ 07033

Dear Ms. Nehring:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Eulexin® (flutamide) Capsules, USP

NDA Number: 18-554

Supplement Number: S-022

Date of Supplement: March 6, 2001

Date of Receipt: March 7, 2001

This supplemental application, submitted as a "Supplement - Changes Being Effected" (CBE) supplement, proposes the following changes: revisions to the Patient Information Sheet in the **Who should not take the Eulexin product?** section (to make consistent with the package insert revisions submitted on March 5, 2001) and the **Where can I get further support?** section.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on May 6, 2001 in accordance with 21 CFR 314.101(a).

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Jeanine Best, M.S.N., R.N.
Regulatory Project Manager
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

/s/

Jeanine Best
3/7/01 02:11:23 PM

APPEARS THIS WAY
ON ORIGINAL