CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-261/S034
21-192/S008

Trade Name: Lescol Capsules & Lescol XL E-R Tablets

Generic Name: (fluvastatin sodium)

Sponsor: Novartis Pharmaceuticals Corporation

Approval Date: January 2, 2005

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S034

21-192/S008

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S034

21-192/S008

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-261/S-034
NDA 21-192/S-008

Novartis Pharmaceuticals Corporation
Attention: Lisa N. Pitt, PharmD
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, NJ 07936-1080

Dear Dr. Pitt:

Please refer to your supplemental new drug applications dated January 19, 2004, received January 20, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lescol (fluvastatin sodium) Capsules and Lescol XL (fluvastatin sodium) Extended-Release Tablets, respectively.

We acknowledge receipt of your submissions dated August 19 and October 13, 2004.

Your submissions of August 19, 2004 constituted a complete response to our July 20, 2004 action letter.

These supplemental new drug applications provide for the implementation of a Patient Package Insert (PPI).

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the patient package insert). Submit the content of labeling in electronic format as described in 21 CFR 314.50(l)(5) and in the format described at the following website: http://www.fda.gov/oc/datacouncil/spl.html.

Approval of these submissions by FDA is not required before the labeling is used.

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

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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, call Margaret Simoneau, Regulatory Project Manager, at (301) 301-827-6411.

Sincerely,

{See appended electronic signature page}

David G. Orloff, MD
Director
Division of Metabolic & Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Patient Package Insert

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Mary Parks
1/5/05 09:47:26 AM
for Dr. Orloff

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S034

21-192/S008

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 20-261/S-034
NDA 21-192/S-008

Novartis Pharmaceuticals Corporation
Attention: Lisa N. Pitt, PharmD
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey
07936-1080

Dear Dr. Pitt:

Please refer to your supplemental new drug applications dated January 19, 2004, received January 20, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lescol (fluvastatin sodium) Capsules (NDA 20-261) and Lescol XL (fluvastatin sodium) Extended-Release Tablets (NDA 21-192).

These supplemental new drug applications propose to implement a Patient Package Insert (PPI) for Lescol and Lescol XL.

Additionally, we refer to our July 14, 2004, email which provided draft labeling revised by the Agency.

We completed our review of these applications and they are approvable. Before these applications may be approved, however, you must submit draft labeling incorporating the revisions recommended in our email of July 14, 2004. The revised PPI is enclosed with this letter.

In addition, all previous revisions as, reflected in the most recently approved package insert, must be included. To facilitate review of your submission, provide a highlighted or marked-up copy that shows the changes.

If additional information relating to the safety or effectiveness of these drugs becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend these application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the applications under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

These products may be considered misbranded under the Federal Food, Drug, and Cosmetic Act if they are marketed with these changes before approval of these supplemental applications.

If you have any questions, call Margaret Simoneau, M.S. R.Ph., Regulatory Project Manager, at (301)827-6411.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

PATIENT INFORMATION

LESCOL® [lĕs-cŏl]
(fluvastatin sodium) **capsules**

and

LESCOL® [lĕs-cŏl] XL
(fluvastatin sodium) **extended-release tablets**

Read the Patient Information that comes with LESCOL or LESCOL XL before you start taking it, and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

If you have any questions about LESCOL or LESCOL XL, ask your doctor or pharmacist.

What are LESCOL and LESCOL XL?

LESCOL and LESCOL XL are prescription medicines called "statins" that lower cholesterol in your blood. They lower the "bad" cholesterol and triglycerides in your blood. They can raise your "good" cholesterol as well.

LESCOL and LESCOL XL are for people whose cholesterol does not come down enough with exercise and a low-fat diet alone.

LESCOL and LESCOL XL may be used in patients with heart disease (coronary artery disease) to:

- lower the chances of heart problems which would require procedures to help restore blood flow to the heart.
- slow the buildup of too much cholesterol in the arteries of the heart.

Treatment with LESCOL or LESCOL XL has not been shown to prevent heart attacks or stroke.

LESCOL and LESCOL XL have the same active ingredient, fluvastatin. However, LESCOL is a capsule that is taken one or two times a day and LESCOL XL is an extended-release tablet that is only taken one time a day.

Who should not take LESCOL or LESCOL XL?

Do not take LESCOL or LESCOL XL if you:

- **are pregnant or think you may be pregnant, or are planning to become pregnant.** LESCOL and LESCOL XL may harm your unborn baby. If you get pregnant, stop taking LESCOL or LESCOL XL and call your doctor right away.
- **are breast feeding.** LESCOL and LESCOL XL can pass into your breast milk and may harm your baby
- **have liver problems**

- **are allergic to LESCOL or LESCOL XL or any of its ingredients.** The active ingredient in LESCOL and LESCOL XL is fluvastatin. See the end of this leaflet for a complete list of ingredients in LESCOL and LESCOL XL.

LESCOL and LESCOL XL have not been studied in children under 18 years of age. LESCOL and LESOL XL are not recommended for use in children.

Before taking LESCOL or LESCOL XL, tell your doctor if you:

- have muscle aches or weakness
- drink more than 2 glasses of alcohol daily
- have diabetes
- have a thyroid problem
- have kidney problems

Some medicines should not be taken with LESCOL or LESCOL XL. Tell your doctor about all the medicines you take, including prescription and non-prescription medicine, vitamins and herbal supplements. LESCOL and LESCOL XL and certain other medicines can interact causing serious side effects. Especially tell your doctor if you take medicines for:

- your immune system
- cholesterol
- infections
- heart failure
- seizures
- diabetes
- heartburn or stomach ulcers

Know all the medicines you take. Keep a list of them with you to show your doctor and pharmacist.

How should I take LESCOL or LESCOL XL?

- Take LESCOL or LESCOL XL exactly as prescribed. Your doctor will prescribe the one that is right for you. Do not change your dose or stop LESCOL or LESCOL XL without talking to your doctor. Your doctor may do blood tests to check your cholesterol levels during treatment with LESCOL and LESCOL XL. Your dose of LESCOL or LESCOL XL may be changed based on these blood test results.
- Take LESCOL capsules or LESCOL XL tablets at the same time every evening. Sometimes LESCOL capsules are taken every morning also. LESCOL and LESCOL XL can be taken with or without food.
- LESCOL XL tablets must be swallowed whole with a liquid. **Do not break, crush or chew LESCOL XL tablets or open Lescol capsules.** Tell your doctor if you cannot swallow tablets whole. You may need LESCOL capsules or a different medicine instead of LESCOL XL tablets.
- Your doctor should start you on a low-fat and low-cholesterol diet before giving you LESCOL or LESCOL XL. Stay on this low-fat and low-cholesterol diet while taking LESCOL or LESCOL XL.
- If you miss a dose of LESCOL or LESCOL XL, take it as soon as you remember. Do not take Lescol or Lescol XL if it has been more than 12 hours since your last dose. Wait and take the next dose at your regular time. **Do not take 2 doses of Lescol or Lescol XL at the same time.**
- If you take too much LESCOL or LESCOL XL or overdose, call your doctor or Poison Control Center right away. Or go to the nearest emergency room.

What should I avoid while taking LESCOL or LESCOL XL?

- Talk to your doctor before you start any new medicines. This includes prescription and non-prescription medicines, vitamins and herbal supplements. LESCOL and LESCOL XL and certain other medicines can interact causing serious side effects.
- Do not get pregnant. If you get pregnant, stop taking LESCOL or LESCOL XL right away and call your doctor.

What are the possible side effects of LESCOL and LESCOL XL?

LESCOL and LESCOL XL may cause serious side effects, including:

- **muscle problems.** These serious muscle problems can sometimes lead to kidney problems, including kidney failure. You have a higher chance for muscle problems if you are taking certain other medicines with LESCOL or LESCOL XL.
- **liver problems.** Your doctor may do blood tests to check your liver before you start taking LESCOL or LESCOL XL, and while you are taking one of them.

Call your doctor right away if you have:

- muscle problems like weakness, tenderness, or pain that happen without a good reason, especially if you also have a fever or feel more tired than usual
- nausea and vomiting
- passing brown or dark-colored urine
- you feel more tired than usual
- your skin and whites of your eyes get yellow
- stomach pain

The most common side effects with LESCOL or LESCOL XL are headache, upset stomach and stomach pain, diarrhea, flu-like symptoms, muscle pain, sinus infection, tiredness, or trouble sleeping.

Talk to your doctor or pharmacist if you have side effects that bother you or that will not go away.

These are not all the side effects with LESCOL and LESCOL XL. Ask your doctor or pharmacist for a complete list.

How should I store LESCOL and LESCOL XL?

- Store LESCOL and LESCOL XL at room temperature, 59° to 86° F (15° to 30° C).

- Do not keep medicine that is out of date or that you no longer need.
- **Keep LESCOL and LESCOL XL out of the reach of children.** Be sure that if you throw medicines away, it is out of the reach of children.

General information about LESCOL and LESCOL XL

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use LESCOL or LESCOL XL for a condition for which it was not prescribed. Do not give LESCOL or LESCOL XL to other people, even if they have the same problem you have. It may harm them.

This leaflet summarizes the most important information about LESCOL and LESCOL XL. If you would like more information, talk with your doctor. For information that is written for health professionals, ask your doctor or pharmacist or call **1-888-669-6682.**

What are the ingredients in LESCOL and LESCOL XL?

Active Ingredient: fluvastatin sodium

Inactive Ingredients:

LESCOL Capsules: gelatin, magnesium stearate, microcrystalline cellulose, pregelatinized starch (corn), red iron oxide, sodium laurel sulfate, talc, titanium dioxide, yellow iron oxide, and other ingredients. The capsules may also contain benzyl alcohol, black iron oxide, butylparaben, carboxymethylcellulose sodium, edetate calcium disodium, methylparaben, propylparaben, silicon dioxide, and sodium propionate.

LESCOL XL Tablets: microcrystalline cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, potassium bicarbonate, povidone, magnesium stearate, iron oxide yellow, titanium dioxide and polyethylene glycol 8000.

Rx only

[Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936]

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Mary Parks
7/20/04 12:47:57 PM
for Dr. Orloff

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S034

21-192/S008

LABELING

PATIENT INFORMATION

LESCOL® [lĕs-cŏl]
(fluvastatin sodium)
Capsules

and

LESCOL® [lĕs-cŏl] XL
(fluvastatin sodium)
Extended-release tablets

Read the Patient Information that comes with LESCOL or LESCOL XL before you start taking it, and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

If you have any questions about LESCOL or LESCOL XL, ask your doctor or pharmacist.

What are LESCOL and LESCOL XL?

LESCOL and LESCOL XL are prescription medicines called "statins" that lower cholesterol in your blood. They lower the "bad" cholesterol and triglycerides in your blood. They can raise your "good" cholesterol as well.

LESCOL and LESCOL XL are for people whose cholesterol does not come down enough with exercise and a low-fat diet alone.

LESCOL and LESCOL XL may be used in patients with heart disease (coronary artery disease) to:

- lower the chances of heart problems which would require procedures to help restore blood flow to the heart.
- slow the buildup of too much cholesterol in the arteries of the heart.

Treatment with LESCOL or LESCOL XL has not been shown to prevent heart attacks or stroke.

LESCOL and LESCOL XL have the same active ingredient, fluvastatin. However, LESCOL is a capsule that is taken one or two times a day and LESCOL XL is an extended-release tablet that is only taken one time a day.

Who should not take LESCOL or LESCOL XL?

Do not take LESCOL or LESCOL XL if you:

- **are pregnant or think you may be pregnant, or are planning to become pregnant.** LESCOL and LESCOL XL may harm your unborn baby. If you get pregnant, stop taking LESCOL or LESCOL XL and call your doctor right away.
- **are breast-feeding.** LESCOL and LESCOL XL can pass into your breast milk and may harm your baby
- **have liver problems**

- **are allergic to LESCOL or LESCOL XL or any of its ingredients.** The active ingredient in LESCOL and LESCOL XL is fluvastatin. See the end of this leaflet for a complete list of ingredients in LESCOL and LESCOL XL.

LESCOL and LESCOL XL have not been studied in children under 18 years of age. LESCOL and LESOL XL are not recommended for use in children.

Before taking LESCOL or LESCOL XL, tell your doctor if you:

- have muscle aches or weakness
- drink more than 2 glasses of alcohol daily
- have diabetes
- have a thyroid problem
- have kidney problems

Some medicines should not be taken with LESCOL or LESCOL XL. Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements. LESCOL and LESCOL XL and certain other medicines can interact causing serious side effects. Especially tell your doctor if you take medicines for:

- your immune system
- cholesterol
- infections
- heart failure
- seizures
- diabetes
- heartburn or stomach ulcers

Know all the medicines you take. Keep a list of all the medicines you take with you to show your doctor and pharmacist.

How should I take LESCOL or LESCOL XL?

- Take LESCOL or LESCOL XL exactly as prescribed. Your doctor will prescribe the one that is right for you. Do not change your dose or stop LESCOL or LESCOL XL without talking to your doctor. Your doctor may do blood tests to check your cholesterol levels during treatment with LESCOL and LESCOL XL. Your dose of LESCOL or LESCOL XL may be changed based on these blood test results.
- Take LESCOL capsules or LESCOL XL tablets at the same time every evening. Sometimes LESCOL capsules are also taken every morning. LESCOL and LESCOL XL can be taken with or without food.
- LESCOL XL tablets must be swallowed whole with a liquid. **Do not break, crush or chew LESCOL XL tablets or open Lescol capsules.** Tell your doctor if you cannot swallow tablets whole. You may need LESCOL capsules or a different medicine instead of LESCOL XL tablets.
- Your doctor should start you on a low-fat and low-cholesterol diet before giving you LESCOL or LESCOL XL. Stay on this low-fat and low-cholesterol diet while taking LESCOL or LESCOL XL.
- If you miss a dose of LESCOL or LESCOL XL, take it as soon as you remember. Do not take Lescol or Lescol XL if it has been more than 12 hours since your last dose. Wait and take the next dose at your regular time. **Do not take 2 doses of Lescol or Lescol XL at the same time.**
- If you take too much LESCOL or LESCOL XL or overdose, call your doctor or Poison Control Center right away. Or, go to the nearest emergency room.

What should I avoid while taking LESCOL or LESCOL XL?

- Talk to your doctor before you start any new medicines. This includes prescription and non-prescription medicines, vitamins and herbal supplements. LESCOL and LESCOL XL and certain other medicines can interact causing serious side effects.
- Do not get pregnant. If you get pregnant, stop taking LESCOL or LESCOL XL right away and call your doctor.

What are the possible side effects of LESCOL and LESCOL XL?

When taking LESCOL and LESCOL XL, some patients may develop serious side effects, including:

- **muscle problems.** These serious muscle problems can sometimes lead to kidney problems, including kidney failure. You have a higher chance for muscle problems if you are taking certain other medicines with LESCOL or LESCOL XL.
- **liver problems.** Your doctor may do blood tests to check your liver before you start taking LESCOL or LESCOL XL, and while you are taking one of them.

Call your doctor right away if you have:

- muscle problems like weakness, tenderness, or pain that happen without a good reason, especially if you also have a fever or feel more tired than usual
- nausea and vomiting
- passing brown or dark-colored urine
- you feel more tired than usual
- your skin and whites of your eyes get yellow
- stomach pain

The most common side effects of LESCOL or LESCOL XL are headache, upset stomach and stomach pain, diarrhea, flu-like symptoms, muscle pain, sinus infection, tiredness, or trouble sleeping. These side effects are usually mild and may go away.

Talk to your doctor or pharmacist if you have side effects that bother you or that will not go away.

These are not all the side effects of LESCOL and LESCOL XL. Ask your doctor or pharmacist for a complete list.

How should I store LESCOL and LESCOL XL?

- Store LESCOL and LESCOL XL at room temperature, 59° to 86° F (15° to 30° C).
- Do not keep medicine that is out of date or that you no longer need.
- **Keep LESCOL and LESCOL XL out of the reach of children.** Be sure that if you throw medicines away, it is out of the reach of children.

General information about LESCOL and LESCOL XL

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use LESCOL or LESCOL XL for a condition for which it was not prescribed. Do not give LESCOL or LESCOL XL to other people, even if they have the same problem you have. It may harm them.

This leaflet summarizes the most important information about LESCOL and LESCOL XL. If you would like more information, talk with your doctor. For information that is written for health professionals, ask your doctor or pharmacist or call **1-888-669-6682.**

What are the ingredients in LESCOL and LESCOL XL?

Active Ingredient: fluvastatin sodium

Inactive Ingredients:

LESCOL Capsules: gelatin, magnesium stearate, microcrystalline cellulose, pregelatinized starch (corn), red iron oxide, sodium lauryl sulfate, talc, titanium dioxide, yellow iron oxide, and other ingredients. The capsules may also contain benzyl alcohol, black iron oxide, butylparaben, carboxymethylcellulose sodium, edetate calcium disodium, methylparaben, propylparaben, silicon dioxide, and sodium propionate.

LESCOL XL Tablets: microcrystalline cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, potassium bicarbonate, povidone, magnesium stearate, yellow iron oxide, titanium dioxide and polyethylene glycol 8000.

Rx only

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936
August 2004
89023001
T2004-60

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S034

21-192/S008

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Division of Metabolic & Endocrine Drug Products

Labeling Review

Application Number: NDA 20-261/S-034

NDA 21-192/S-008

Name of Drug: Lescol (fluvastatin sodium) Capsules, 20 mg, 40 mg

Lescol XL (fluvastatin sodium) Extended-Release Tablets, 80 mg

Sponsor: Novartis Pharmaceuticals Corporation

Submission Date: March 24, 2005 Final Printed labeling submission (in EDR)

Background and Summary:

Lescol is indicated in:

- Hypercholesterolemia (heterozygous familial and non familial) and Mixed Dyslipidemia
- Atherosclerosis

The last approved labeling for NDA 20-261/S-033 (Lescol Capsules) and NDA 21-192/S-005 (Lescol XL Extended-Release Tablets), were approved on May 27, 2003, (Package Identifier #T2003340, 89011106). These supplemental new drug applications provided for a new indication, based on the results of the Lescol Intervention Prevention Study (LIPS), for the use of fluvastatin in patients with coronary heart disease to reduce the risk of undergoing coronary revascularization procedures.

Review:

NDA 20-261/S-034 (Lescol Capsules) and NDA 21-192/S-008 (Lescol XL Tablets) are supplemental new drug applications that implement a new Patient Package Insert (PPI). There are no changes to the package insert (PI) with the implementation of the PPI.

Conclusion:

The FPL (T2005-13, 5000291, January 2005) was compared to the labeling that was approved on January 5, 2005 (Identifier T2004-60, 89023001, August 2004). The identifier, revision date and formatting have been revised. These are acceptable and appropriate changes. An Acknowledge and Retain letter will issue.

Reviewed by: M.A. Simoneau, R.Ph., Regulatory Project Manager

(See appended electronic signature page)

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/s/

Margaret Simoneau
4/27/05 02:28:37 PM
CSO

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: April 14, 2004

TO: David Orloff, M.D., Director
Division of Metabolic and Endocrine Drug Products, HFD-510

VIA: Margaret Simoneau, R.Ph., Regulatory Health Project Manager,
Division of Metabolic and Endocrine Drug Products, HFD-510

FROM: Jeanine Best, M.S.N., R.N., P.N.P.
Patient Product Information Specialist
Division of Surveillance, Research, and Communication Support
HFD-410

THROUGH: Gerald Dal Pan, M.D., M.H.S., Director
Division of Surveillance, Research, and Communication Support
HFD-410

SUBJECT: ODS/DSRCS Review of the Patient Labeling for Lescol Capsules and Lescol XL Extended-Release Tablets (fluvastatin sodium), sNDAs 20-261/S-034 and 21-192/S-008

Background and Summary

The attached patient labeling represents the revised risk communication materials for Lescol Capsules and Lescol XL Extended-Release Tablets (fluvastatin sodium), sNDAs 20-261/S-034 and 21-192/S-008. It has been reviewed by our office and by DDMAC. We have simplified the wording, made it consistent with the PI, removed promotional language and other unnecessary information (the purpose of patient information leaflets is to enhance appropriate use and provide important risk information about medications), and put it in the format that we are recommending for all patient information. Our proposed changes are known through research and experience to improve risk communication to a broad audience of varying educational backgrounds. These revisions are based on draft labeling submitted by the sponsor on January 19, 2004. Patient information should always be consistent with the prescribing information. All future changes to the PI should also be reflected in the PPI.

Comments to the review division are bolded, underlined and italicized. We can provide marked-up and clean copies of the revised documents in Word if requested by the review division. Please call is if you have any questions

PATIENT INFORMATION

4 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 20-261 5034

21-192/5008

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/s/

Jeanine Best
4/14/04 08:54:07 AM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
4/14/04 08:57:45 AM
DRUG SAFETY OFFICE REVIEWER
for Gerald Dal Pan

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

DATE: April 2, 2004

FROM: Debi Tran, PharmD, Regulatory Reviewer, DDMAC

TO: Jeanine Best, MSN, RN, PNP, Patient Product Information Specialist, ODS

Re: Comments on patient package insert (PPI) for Lescol® Capsules (NDA 20-261) and Lescol XL® Extended-Release Tablets (NDA 21-192)

Thank you for forwarding a copy of the draft PPI to DDMAC. The following comments were based on the draft PPI that was emailed to DDMAC on March 9, 2004.

What are LESCOL and LESCOL XL?
Is the following statement supported by substantial evidence or substantial clinical experience?

b(4)
b(4)
(emphasis added)

The PI states "In patients with neart disease b(4)
b(4)

General information about LESCOL and LESCOL XL
Regarding the second paragraph, we note that "Lescol" was misspelled. Please revise accordingly.

b(4)

We recommend that the sponsor replace with "Lescol and Lescol XL" in the sentence "You can ask your doctor or pharmacist for information about that is written for health professionals." b(4)

b(4)

What are the ingredients in LESCOL and LESCOL XL?
the inactive ingredients for Lescol XL The inactive ingredients are microcrystalline cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, potassium bicarbonate, povidone, magnesium stearate, iron oxide yellow, titanium dioxide, and polyethylene glycol 8000.

We also note that a b(4) doctor b(4)

Should you have any questions concerning my comments, please contact me at 301-827-3887.

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/s/

Debi Tran
4/2/04 12:19:21 PM
DDMAC REVIEWER

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Mail: Office of Drug Safety (ODS) DSRCS
HFD-410/ Attn: Leslie Stephens (7-3235)

FROM:
Margaret Simoneau, R.Ph. (7-6411)/HFD-510

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 2, 2004		20-261/S-034 and 21-192/S-008	SLR	January 19, 2004 (in EDR)

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Lescol (fluvastatin) capsules and Lescol XL Extended-release tablets	Standard	Lipid altering agent (statin)	May 14, 2004

NAME OF FIRM:

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Request review of the January 19, 2004, submission regarding the Patient Package Insert for Lescol and Lescol XL. Please feel free to speak with Dr.William Lubas, Medical Reviewer, regarding this consult @ 7-6374.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Dr. Mary Parks, Deputy Division Director, HFD-510	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER Margaret Simoneau

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/s/

Mary Parks
2/2/04 12:44:06 PM

From: lisa.pitt@pharma.novartis.com
Sent: Monday, July 19, 2004 11:46 AM
To: Simoneau, Margaret A
Subject: Re: NDA 20-261/S-034 and 21-192/S-008 Lescol and Lescol XL Draft PPI #2 (71404)

Dear Margaret,

I have had discussions with my management and have reached the conclusion that an Approvable Letter is the most appropriate course of action at this time, in order to provide our legal colleagues an opportunity to discuss their concerns. I know we had discussed tomorrow morning as a possibility for a brief TC however one of the personnel is not in the office today and I would rather not leave you in limbo.

I do greatly appreciate your flexibility in this matter and please feel free to contact me should you have any questions.

Thanks and kind regards,
Lisa

Lisa N. Pitt, Pharm.D.
CVM Drug Regulatory Affairs
502/121
862-778-3279

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/s/

Margaret Simoneau
7/20/04 09:36:51 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-261/S-034
NDA 21-192/S-008

Novartis Pharmaceuticals Corporation
Attention: Lisa N. Pitt, Pharm.D.
Associate Director, Drug Regulatory Affairs
One Health Plaza
59 Route 10
East Hanover, NJ 07936-1080

Dear Dr. Pitt:

We acknowledge receipt of your March 24, 2005 submission containing final printed labeling in response to our January 5, 2005 letter approving your supplemental new drug application for Lescol (fluvastatin sodium) Capsules, Lescol XL (fluvastatin sodium) Extended-release Tablets.

We have reviewed the labeling that you submitted in accordance with our January 5, 2005 letter and we find it acceptable.

If you have any questions, please call me at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

Margaret Simoneau, M.S., R.Ph.
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Margaret Simoneau
4/27/05 02:00:34 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-261/S-034
NDA 21-192/S-008

PRIOR APPROVAL SUPPLEMENT

Novartis Pharmaceuticals Corporation
Attn: Lisa N. Pitt, Pharm.D.
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Pitt:

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 Products:	Lescol® (fluvastatin sodium) Capsules Lescol XL® (fluvastatin sodium) Extended–Release Tablets
NDA Numbers:	20-261 21-192
Supplement numbers:	S-034 S-008
Date of supplements:	January 19, 2004
Date of receipts:	January 20, 2004

This supplemental application proposes a Patient Package Insert (PPI) as an addition to the approved product labeling.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on March 20, 2004 in accordance with 21 CFR 314.101(a). If the application is filed, the goal date will be July 20, 2004.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic & Endocrine Drug Products, HFD-510
Attention: Fishers Document Room, 8B45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question, call me at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

Margaret Simoneau, M.S., R.Ph.
Regulatory Project Manager
Division of Metabolic & Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Margaret Simoneau
2/2/04 10:14:35 AM