CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 21-411/S-001

Trade Name: Strattera Capsules

Generic Name: atomoxetine hydrochloride

Sponsor: Eli Lilly and Company

Approval Date: January 17, 2003

Indications: For the treatment of Attention-deficit/Hyperactivity Disorder (ADHD)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21-411/S-001

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21-411/S-001

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-411

Eli Lilly and Company
Attention: Robin P. Wojcieszek, R.Ph.
Senior Regulatory Scientist
Lilly Corporate Center
Indianapolis, IN 46285

Dear Ms.Wojcieszek:

Please refer to your supplemental new drug application (NDA) dated December 11, 2002, received December 13, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Strattera™ (atomoxetine hydrochloride) Capsules.

This supplemental new drug application provides for a patient package insert (PPI) as part of the labeling.

We refer to two facsimile communications dated December 13 and December 18, 2002, concerning the wording of the PPI labeling.

We also refer to the January 16, 2003, telephone conversation between Ms. Robin Wojcieszek, Lilly Senior Regulatory Scientist, and Ms. Anna Marie H. Weikel, Senior Project Manager of this Division, during which the final PPI labeling was agreed upon.

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 enclosed PPI 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 agreed upon enclosed labeling (text for the patient package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 NDA 21-411/S-001." Approval of this submission by FDA is not required before the labeling is used.

If you should have any questions, please call Ms. Anna Marie H. Weikel, R.Ph., Senior Regulatory Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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

/s/

Russell Katz
1/17/03 08:17:30 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21-411/S-001

LABELING

[FDA APPROVED PPI FOR NDA 21-411/S-001
ATTACHMENT TO APPROVAL LETTER]

NL 3740 AMP

INFORMATION FOR PATIENTS OR THEIR PARENTS OR CAREGIVERS

STRATTERA™
(atomoxetine HCl)

Read this information before you start taking STRATTERA (Stra-TAIR-a). Read this information you get each time you get more STRATTERA. There may be new information. This information does not take the place of talking to your doctor about your medical condition or treatment.

What is STRATTERA?

STRATTERA is a non-stimulant medicine used to treat Attention-Deficit/Hyperactivity Disorder (ADHD). STRATTERA contains atomoxetine hydrochloride, a selective norepinephrine reuptake inhibitor. Your doctor has prescribed this medicine as part of an overall treatment plan to control your symptoms of ADHD.

What is ADHD?

ADHD has 3 main types of symptoms: inattention, hyperactivity, and impulsiveness. Symptoms of inattention include not paying attention, making careless mistakes, not listening, not finishing tasks, not following directions, and being easily distracted. Symptoms of hyperactivity and impulsiveness include fidgeting, talking excessively, running around at inappropriate times, and interrupting others. Some patients have more symptoms of hyperactivity and impulsiveness while others have more symptoms of inattentiveness. Some patients have all 3 types of symptoms.

Symptoms of ADHD in adults may include a lack of organization, problems starting tasks, impulsive actions, daydreaming, daytime drowsiness, slow processing of information, difficulty learning new things, irritability, lack of motivation, sensitivity to criticism, forgetfulness, low self-esteem, and excessive effort to maintain some organization. The symptoms shown by adults who primarily have attention problems but not hyperactivity have been commonly described as Attention-Deficit Disorder (ADD).

Many people have symptoms like these from time to time, but patients with ADHD have these symptoms more than others their age. Symptoms must be present for at least 6 months to be certain of the diagnosis.

Who should NOT take STRATTERA?

Do not take STRATTERA if:

- you took a medicine known as a monoamine oxidase inhibitor (MAOI) in the last 2 weeks. An MAOI is a medicine sometimes used for depression and other mental problems. Some names of MAOI medicines are Nardil® (phenelzine sulfate) and Parnate® (tranylcypromine sulfate). Taking STRATTERA with an MAOI could cause serious side effects or be life-threatening.
- you have narrow angle glaucoma, an eye disease.
- you are allergic to STRATTERA or any of its ingredients. The active ingredient is atomoxetine. The inactive ingredients are listed at the end of this leaflet.

What should I tell my doctor before taking STRATTERA?

Talk to your doctor before taking STRATTERA if you:

- have or had liver problems. You may need a lower dose.
- have high blood pressure. STRATTERA can increase blood pressure.
- have problems with your heart or an irregular heartbeat. STRATTERA can increase heart rate (pulse).
- have low blood pressure. STRATTERA can cause dizziness or fainting in people with low blood pressure.

Tell your doctor about all the medicines you take or plan to take, including prescription and non-prescription medicines, dietary supplements, and herbal remedies. Your doctor will decide if you can take STRATTERA with your other medicines.

Certain medicines may change the way your body reacts to STRATTERA. These include medicines used to treat depression [like Paxil® (paroxetine) and Prozac® (fluoxetine)], and certain other medicines (like quinidine). Your doctor may need to change your dose of STRATTERA if you are taking it with these medicines.

STRATTERA may change the way your body reacts to oral or intravenous albuterol (or drugs with similar actions), but the effectiveness of these drugs will not be changed. Talk with your doctor before taking STRATTERA if you are taking albuterol.

How should I take STRATTERA?

- Take STRATTERA according to your doctor's instructions. This is usually taken 1 or 2 times a day (morning and late afternoon/early evening).
- You can take STRATTERA with or without food.
- If you miss a dose, take it as soon as possible, but do not take more than your total daily dose in any 24-hour period.
- Taking STRATTERA at the same time each day may help you remember.
- STRATTERA is available in several dosage strengths: 10, 18, 25, 40, and 60 mg.

Call your doctor right away if you take more than your prescribed dose of STRATTERA.

Other important safety information about STRATTERA

Use caution when driving a car or operating heavy machinery until you know how STRATTERA affects you.

Talk to your doctor if you are:
- pregnant or planning to become pregnant
- breast-feeding. We do not know if STRATTERA can pass into your breast milk.

What are the possible side effects of STRATTERA?

The most common side effects of STRATTERA used in teenagers and children over 6 years old are:
- upset stomach
- decreased appetite
- nausea or vomiting
- dizziness
- tiredness
- mood swings

Weight loss may occur after starting STRATTERA. It is not known if growth will be slowed in children who use STRATTERA for a long period of time. Your doctor will watch your weight and height. If you are not growing or gaining weight as expected, your doctor may change your treatment of STRATTERA.

The most common side effects of STRATTERA used in adults are:
- constipation
- dry mouth
- nausea
- decreased appetite
- dizziness
- problems sleeping
- sexual side effects
- problems urinating
- menstrual cramps

Stop taking STRATTERA and call your doctor right away if you get swelling or hives. STRATTERA can cause a serious allergic reaction in rare cases.

This is not a complete list of side effects. Talk to your doctor if you develop any symptoms that concern you.

General advice about STRATTERA

STRATTERA has not been studied in children under 6 years old.

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use STRATTERA for a condition for which it was not prescribed. Do not give STRATTERA to other people, even if they have the same symptoms you have.

This leaflet summarizes the most important information about STRATTERA. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information on STRATTERA that is written for health professionals. You can also call 1-800-Lilly-Rx (1-800-545-5979) or visit our website at www.strattera.com.

What are the ingredients in STRATTERA?

Active ingredient: atomoxetine.
Inactive ingredients: pregelatinized starch, dimethicone, gelatin, sodium lauryl sulfate, FD&C Blue No. 2, synthetic yellow iron oxide, titanium dioxide, and edible black ink.

Store STRATTERA at room temperature.

This patient information summary has been approved by the US Food and Drug Administration.

Literature issued XXXX

Eli Lilly and Company
Indianapolis, IN 46285

www.strattera.com

NL 3740 AMP PRINTED IN USA

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21-411/S-001

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-411/S-001

Eli Lilly and Company
Attention: Robin Wojcieszek, R.Ph.
Sr. Regulatory Scientist
U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Ms.Wojcieszek:

We acknowledge the receipt of your March 18, 2003, submission containing final printed labeling in response to our supplemental approval letter.

We have reviewed the labeling (PV 3752 AMP and PV 3740 AMP) that you submitted in accordance with our January 17, 2003, letter, and we find it acceptable.

If you should have any questions, please call Ms. Anna Marie H. Weikel, R.Ph., Senior Regulatory Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Russell Katz
5/2/03 08:41:19 AM

Division of Neuropharmacological Drug Products
Regulatory Project Manager Labeling Review

NDA Number: 21-411/S-001

Drug: Strattera™ (atomoxetine hydrochloride) Capsules

Sponsor: Eli Lilly Company

Material Reviewed:
1) FPL Submission dated 3/18/03
2) FDA approved labeling dated January 17, 2003 for S-001

Submission Date: March 18, 2003

Receipt Date: March 19, 2003

Background:
NDA 21-411/S-001 which provided for the patient package insert (PPI) for Strattera® was approved on January 17, 2003, with draft labeling. FPL was submitted on March 18, 2003. In addition to the proposed PPI, however, this supplement also proposed a statement to be added to the package insert (PI) to reflect for the addition of a PPI so that prescribers would be aware of it.

Review:
A side-by-side comparison between what was approved in draft, NL 3740 AMP, and the submitted FPL, PV3740, reveals that there are stylistic changes in the PPI (see attachment).

However, the following statement, 'Patients should read Information for Patients before starting therapy with STRATTERA and when the prescription is renewed.', has been added to the Precautions section of professional package insert as a cross reference, as stated in the cover letter of the FPL submission

Conclusions:
I therefore recommend that an 'Acknowledge and Retain' letter be issued with the concurrence of the review team for the additional change described above.

_____
Anna Marie H. Weikel, RPh
Regulatory Project Manager

Supervisory Concurrence: _____
Robbin Nighswander, R.Ph.
Supervisory Project Manager

~~[FDA-APPROVED PPI FOR NDA 21-411/S-001
ATTACHMENT TO APPROVAL LETTER]~~

~~NL~~PV 3740 AMP

INFORMATION FOR PATIENTS OR THEIR PARENTS OR CAREGIVERS

STRATTERA™
(atomoxetine HCl)

Read this information before you start taking ~~STRATTERA (Stra-TAIR-a).~~STRATTERA (Stra-TAIR-a). Read this information you get each time you get more STRATTERA. There may be new information. This information does not take the place of talking to your doctor about your medical condition or treatment.

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What is ADHD?

ADHD has 3 main types of symptoms: inattention, hyperactivity, and impulsiveness. Symptoms of inattention include not paying attention, making careless mistakes, not listening, not finishing tasks, not following directions, and being easily distracted. Symptoms of hyperactivity and impulsiveness include fidgeting, talking excessively, running around at inappropriate times, and interrupting others. Some patients have more symptoms of hyperactivity and impulsiveness while others have more symptoms of inattentiveness. Some patients have all 3 types of symptoms.

Symptoms of ADHD in adults may include a lack of organization, problems starting tasks, impulsive actions, daydreaming, daytime drowsiness, slow processing of information, difficulty learning new things, irritability, lack of motivation, sensitivity to criticism, forgetfulness, low self-esteem, and excessive effort to maintain some organization. The symptoms shown by adults who primarily have attention problems but not hyperactivity have been commonly described as Attention-Deficit Disorder (ADD).

Many people have symptoms like these from time to time, but patients with ADHD have these symptoms more than others their age. Symptoms must be present for at least 6 months to be certain of the diagnosis.

Who should NOT take STRATTERA?

Do not take STRATTERA if:

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- sexual side effects
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This patient information summary has been approved by the US Food and Drug Administration.

Literature issued ~~XXXX~~January 17, 2003

Eli Lilly and Company
Indianapolis, IN 46285

www.strattera.com

~~NL~~PV 3740 AMP PRINTED IN USA

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~~/s/~~

~~Russell Katz~~
~~1/17/03 08:17:30 AM~~

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/s/

Anna-Marie Homonnay
4/16/03 03:11:46 PM
CSO

Robbin Nighswander
4/25/03 11:06:39 AM
CSO

MEMORANDUM

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

DATE: January 16, 2003

FROM: Thomas P. Laughren, M.D.
Team Leader, Psychiatric Drug Products
Division of Neuropharmacological Drug Products
HFD-120

SUBJECT: Strattera (atomoxetine) Patient Package Insert (PPI)

TO: File, NDA 21-411/S-001
[Note: This memo should be filed with the 12-11-02 original submission of this supplement.]

-This 12-11-02 supplement (S-001) is simply a formal submission by Lilly of the PPI that was mutually agreed to by the Division and Lilly at the time the approval package for the NDA was being assembled.

-This mutually agreed to version of the PPI was included in the approval package for this NDA, however, Dr. Temple felt this version was not ready for approval. Thus, we sent our version of the PPI back to DDMAC (12-6-02) for a second review [Note: Lilly's originally proposed PPI had been reviewed earlier by DDMAC, and some, but not all, of their suggested changes had been incorporated.]

-DDMAC provided us with an alternative version of the PPI on 12-13-02, and we submitted this directly to Lilly on 12-13-02 for their response.

-Lilly responded on 12-18-02 with an alternative proposal that included a number of revisions to DDMAC's proposed version, some minor but some more substantial. I responded in a 12-19-02 e-mail that I agreed with all of Lilly's proposed changes, and this memo is intended to formalize my views on this revised version.

-Following are comments on some of the more substantial changes proposed by Lilly:

-Under [ ] DDMAC had deleted the reference to this drug being a[ ] [ ] Lilly want to add this information back in, as well as provide some brief characterization of the drug.

-Comment: I agree that both changes are useful.

-DDMAC had deleted the section [ ]' Lilly added this back in, arguing that this is useful information to patients and their families.

-Comment: Having a section describing the illness for which the drug is useful is standard for ADHD and all other PPIs in DNDP. Thus, I agree with keeping this section.

-DDMAC had added language suggesting that when [redacted]. Lilly correctly pointed out that this is not what labeling recommends. Rather, labeling suggests that the dose of Strattera may need to be adjusted.

-Comment: Lilly is, of course, correct, and no purpose would be served by giving false information in the PPI.

-DDMAC had also changed the advice about [redacted], rather than what the label says, i.e., use caution. Lilly changed the wording back to [redacted]

-Comment: Again, I agree that the PPI should be consistent with labeling.

-DDMAC had added language to the [redacted] Lilly objected to this speculative language.

-Comment: I agree.

-Under '[redacted] DDMAC added the following language to the statement advising that Strattera [redacted]' Lilly found this speculative and inconsistent with the kind of language used in other PPIs.

-Comment: I agree.

Conclusions and Recommendations: As I have indicated, I find all of Lilly's revisions to DDMAC's latest revision acceptable. My major objections, and those of Lilly, are that this version tends to give a negative spin on the drug, includes information that is false and inconsistent with approved labeling, and leaves out some information that is useful to patients. Thus, I recommend that we approve the version that Lilly has proposed on 12-18-02.

cc:
Orig NDA 21-411/S-001
HFD-120/DivFile
HFD-120/TLaughren/RKatz/PAndreason/RGlass/AMHomonnay

DOC: NDA21411.01

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/s/

Thomas Laughren
1/16/03 10:43:25 AM
MEDICAL OFFICER

Homonnay Weikel, Anna M

From: WOJCIESZEK_ROBIN_PITTS@LILLY.COM
Sent: Wednesday, December 18, 2002 9:01 AM
To: homonnaya@cder.fda.gov
Cc: BROPHY_GREGORY_T@LILLY.COM
Subject: Strattera Response
Importance: High

Anna Marie,

I hope all is well. I am back from my vacation.

We have completed our review of the FDA's version of the PPI (12/13/02) and are proposing the attached changes. We have provided both a marked up version along with a clean version.

As Greg had mentioned, if it would be beneficial to have a short phone conversation about the revisions, we can set something up for today or Thursday per availability of your reviewers. I will give you a call later to discuss whether or not we need to schedule something.

Also, would you like us to send in our proposal as an amendment to the NDA? I know that the Division is working toward a quick turnaround so I was not sure if you would like us to send this to the SLR or not. If you could get back to me that would be great.

Thanks for your help and take care,
Robin

Robin Pitts Wojcieszek, R.Ph.
U.S. Regulatory Affairs
Eli Lilly & Co.
317-651-9827 (office) 317-433-2255 (fax)

NL 3740 AMP

INFORMATION FOR PATIENTS OR THEIR PARENTS OR CAREGIVERS [ ]

Lilly Response: For consistency with Ritalin LA® and Concerta®, we have changed the title of the information leaflet.

STRATTERA™ (atomoxetine HCl)

Lilly Response: Modifications to the trade and generic name have been made to be consistent with the USPI.

Read this information before you start taking STRATTERA (Stra-[ ]TAIR-[ ]a). Read [ ] this information you get each time you get more STRATTERA. There may be new information. This information does not take the place of talking to your doctor about your medical condition or treatment.

Lilly Response: We have retained our pronunciation "(Stra-TAIR-a)" of STRATTERA because we feel that it makes the pronunciation clearer. The general population will be more familiar with "air" than with [ ] We have made one other modification for consistency.

What is STRATTERA?

STRATTERA is a non-stimulant medicine used to treat Attention-Deficit-/Hyperactivity Disorder (ADHD). STRATTERA contains atomoxetine hydrochloride, a selective norepinephrine reuptake inhibitor. Your doctor has prescribed this medicine as part of an overall treatment plan to control your symptoms of ADHD. [ ]
[ ]

Lilly Response: We are adding information that helps clarify the difference between methylphenidate stimulant pharmacology and STRATTERA. We are moving the sentence regarding [ ] to be more consistent with other patient labels. We have also made minor modifications to the name of the disease state for consistency with the USPI.

What is ADHD?

ADHD has 3 main types of symptoms: inattention, hyperactivity, and impulsiveness. Symptoms of inattention include not paying attention, making careless mistakes, not listening, not finishing tasks, not following directions, and being easily distracted. Symptoms of hyperactivity and impulsiveness include fidgeting, talking excessively, running around at inappropriate times, and interrupting others. Some patients have more symptoms of hyperactivity and impulsiveness while others have more symptoms of inattentiveness. Some patients have all 3 types of symptoms.

Symptoms of ADHD in adults may include a lack of organization, problems starting tasks, impulsive actions, daydreaming, daytime drowsiness, slow processing of information, difficulty

learning new things, irritability, lack of motivation, sensitivity to criticism, forgetfulness, low self-esteem, and excessive effort to maintain some organization. The symptoms shown by adults who primarily have attention problems but not hyperactivity have been commonly described as Attention-Deficit Disorder (ADD).
Many people have symptoms like these from time to time, but patients with ADHD have these symptoms more than others their age. Symptoms must be present for at least 6 months to be certain of the diagnosis.

Lilly Response: For consistency with Ritalin LA® and Concerta® on educating patients about ADHD, we feel this section is imperative. Especially given high general noncompliance rates, it is important that patients are given at least some good reasons to safely take their prescribed medicines, and not just information that may discourage them from doing so. Further, just as it is important to highlight differences in side effect profiles for adult and children with ADHD, it is important for adult patients to understand the differences in symptoms.

Who should NOT take STRATTERA?

Do not take STRATTERA if:

- you took a medicine known as a monoamine oxidase inhibitor (MAOI) in the last [ ]2 weeks. An MAOI is a medicine sometimes used for depression and other mental problems. Some names of MAOI medicines are Nardil® (phenelzine sulfate) and Parnate® ([ ]tranylcypromine sulfate). Taking STRATTERA with an MAOI[ ]could cause serious side effects or[ ] be life-threatening.

Lilly Response: Lilly accepts the changes with minor modifications.

- you have narrow angle glaucoma, an eye disease. [ ]
[ ]

Lilly Response: The last sentence in the above bullet point was too broad and ambiguous, and not supported by either the data or the PI, as STRATTERA does not [ ]
[ ]

- you are allergic to STRATTERA or any of its ingredients. The active ingredient is atomoxetine. The inactive ingredients are listed at the end of this leaflet.

[ ]

What should I tell my doctor before taking STRATTERA?

Talk to your doctor before taking STRATTERA if you:

Lilly Response: We have deleted the first statement and moved the second statement below the new section heading. These are not contraindications and in most cases, STRATTERA does not [ ] However, we agree that is important for patients to notify their doctors about these conditions so we have therefore framed this accordingly. This is also consistent with Ritalin LA® and Concerta®.

- have or had liver[ ]problems. You may need a lower dose.

Lilly Response: We have deleted [ ] for consistency with the USPI.

- have high blood pressure. STRATTERA can increase blood pressure.
- have problems with your heart or an irregular heartbeat. STRATTERA can increase heart rate (pulse).
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Tell your doctor about all the medicines you take or plan to take, including prescription and non-prescription medicines, dietary supplements, and herbal remedies. Your doctor will decide if you can take STRATTERA with your other medicines.

[ ] Certain medicines may change the way your body reacts to STRATTERA [ ] [ ] These include medicines used to treat depression [ ] [like Paxil® (paroxetine) and Prozac® (fluoxetine)], [ ] and certain other medicines (like quinidine). Your doctor may need to change your dose of [ ] STRATTERA if you are taking [ ] it with [ ] these medicines.

STRATTERA may change the way your body reacts to oral or intravenous albuterol (or drugs with similar actions), but the effectiveness of these drugs will not be changed. Talk with your doctor before taking STRATTERA if you are taking albuterol.

Lilly Response: We accept the FDA modifications but have added "dietary" for consistency with the USPI. We have separated the discussion of potent CYP2D6 inhibitors [Paxil® (paroxetine), Prozac® (fluoxetine), quinidine] from the discussion of albuterol because there are different precautions with these two groups of medications. We have also corrected the discussion of CYP2D6 inhibitors to reflect the recommendations about dosing STRATTERA in the USPI. [ ] [ ] We have inserted a separate section on albuterol that reflects the information in the clinical pharmacology and drug interactions section of the label. Because the clinical pharmacology study referenced in the drug interactions section of the label involved iv (systemic) administration of albuterol, and because cardiovascular effects are minimal with inhaled albuterol, we have focused on iv or oral albuterol in this section

How should I take STRATTERA?

- Take STRATTERA according to your doctor's instructions. This is usually taken 1 or 2 times a day (morning and late afternoon/early evening).
- You can take STRATTERA with or without food.
- If you miss a dose, take it as soon as possible, but do not take more than your total daily dose in any 24-hour period.
- Taking STRATTERA at the same time each day may help you remember.
- STRATTERA is available in several dosage strengths: 10, 18, 25, 40, and 60 mg.

Call your doctor [ ] right away if you take more than your prescribed dose of STRATTERA.

Lilly Response: Lilly accepts the FDA changes. In addition, we have made a couple modifications for clarity and have added the available dosage strengths. We have also deleted the reference to the [ ] as we feel the doctor will have the best information the patient will need to know if he/she has taken more than the safe dose. This instruction is also consistent with patient labeling for Ritalin LA® and Concerta® patient labeling, neither of which instructs patients [ ]

[ ] **Other important safety information about STRATTERA**

[ ] Use caution when driving a car [ ] operating heavy machinery until you know how STRATTERA affects you.

Lilly Response: We have changed the title of this section for clarity and we have reworded the above sentence to be consistent with the USPI.

Talk to your doctor if you are:

- pregnant or planning to become pregnant [ ]
- breast-feeding. We do not know if STRATTERA can pass [ ] into your breast milk [ ] [ ]

Lilly Response: We have made a couple minor modifications and have deleted [ ] [ ] [ ] This is also consistent with Ritalin LA® and Concerta® patient labeling, and with patient labeling for other products with similar data.

What are the possible side effects of STRATTERA?

The most common side effects of STRATTERA used in teenagers and children over 6 years old are:

- upset stomach
- decreased appetite
- nausea [ ] or vomiting
- dizziness
- tiredness
- mood swings

Lilly Response: Lilly accepts the modifications with two minor modifications.

Weight loss may occur after starting STRATTERA. It is not known if growth will be slowed in children who use STRATTERA for a long period of time. Your doctor will watch your weight and height. If you are not growing or gaining weight as expected, your doctor may change your treatment [ ] of STRATTERA.

Lilly Response: Lilly accepts the added paragraph on weight loss with one minor modification.

The most commons side effects of STRATTERA used in adults are:

- constipation
- dry mouth
- nausea
- decreased appetite
- dizziness
- problems sleeping
- sexual side effects
- problems urinating
- menstrual cramps

Lilly Response: Lilly accepts the changes with one minor modification.

Stop taking STRATTERA and call your doctor right away if you get swelling or hives. STRATTERA can cause a serious allergic reaction in rare cases.

This is not a complete list of side effects. Talk to your doctor if you develop any symptoms that concern you.

General advice about STRATTERA

STRATTERA has not been studied in children under 6 years old.

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use STRATTERA for a condition for which it was not prescribed. Do not give STRATTERA to other people, even if they have the same symptoms you have. [ ]

[ ]

This leaflet summarizes the most important information about STRATTERA. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information on STRATTERA that is written for health professionals. You can also call 1-800-Lilly-Rx (1-800-545-5979) or visit our website at www.strattera.com.

Lilly Response: We have added the statement regarding "studied in children under 6 years old" to be more consistent with other patient labeling. We have deleted the sentence [ ] [ ] for consistency with most other patient labeling, and especially with patient labeling for Ritalin LA® and Concerta®. There are no data that are specific to STRATTERA that would support treating it differently from other products with regard to additional context needed for this general piece of advice. We have provided the phone number and website address as requested.

What are the ingredients in STRATTERA?

Active ingredient: atomoxetine.
Inactive ingredients: pregelatinized starch, dimethicone, gelatin, sodium [ ] lauryl sulfate, FD&C Blue No. 2, synthetic yellow iron oxide, titanium dioxide, and edible black ink.

Lilly Response: We accept the modifications and have corrected the spelling of "lauryl."

Store STRATTERA at room temperature.

This patient information summary has been approved by the US Food and Drug Administration.

Literature issued XXXX

Eli Lilly and Company
Indianapolis, IN 46285

www.strattera.com

NL 3740 AMP PRINTED IN USA

Lilly Response: We have retained the information at the bottom of the leaflet to include the approval statement, the issue date, the Lilly signature, the identifying number, the "PRINTED IN USA" line, and the copyright statement.

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

/s/

Anna-Marie Homonnay
1/16/03 09:02:15 AM
CSO

MEMORANDUM

Date: December 18, 2002

To: Dr. Russell Katz
Director
Division of Neuropharmacologic Drug Products
HFD-120

From: Lisa Stockbridge, Ph.D.
Regulatory Reviewer
Division of Drug Marketing, Advertising, and Communications
HFD-42

Re: NDA 21-411
Strattera (atomoxetine HCl)

Material Reviewed: December 11, 2002 proposal of Patient Information leaflet (PPI)

Background: The following PPI is proposed for consistency among the PPIs in the ADHD drug class. It is based upon a template previously provided to HFD-120 for Concerta, Metadate CD, Metadate ER, Methylin ER, Ritalin SR, and dexmethylphenidate. It also reflects the proposals in format, wording, and organization proposed by DSRCS on July 16, 2002, in a review of draft Strattera labeling prior to its approval by DNDP.

Recommendations: DDMAC recommends the following PPI for Strattera.

3 page(s) of draft labeling has been removed from this portion of the review.

Administrative and Correspondence Documents:
Memorandum (12/18/02)

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

/s/

Lisa Stockbridge
12/18/02 01:54:08 PM
CSO

Homonnay Weikel, Anna M

From: Homonnay Weikel, Anna M
Sent: Friday, December 13, 2002 3:13 PM
To: 'BROPHY_GREGORY_T@LILLY.COM'
Cc: Homonnay Weikel, Anna M
Subject: re: FDA Proposed PPI Labeling

Dr. Brophy:
Attached is the FDA labeling proposal for the Strattera PPI pursuant to SLR-001. This proposal was derived in consultation with DDMAC per Dr. Temple's suggestion.

Please indicated your concurrence or any revisions, preferably, no later than mid-next week.

Thank You

Stratteraconsult121302 PPI.doc

Anna Marie H. Weikel, R.Ph.
Divison of Neuropharmacological Drug Products
Office of Drug Evaluation I
FDA Center for Drug Evaluation and Research
Regulatory Affairs Manager
(301) 594-5535
"Go Navy!"

3 page(s) of draft labeling has been removed from this portion of the review.

Administrative and Correspondence Documents:
Email (12/13/02)

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

/s/

Anna-Marie Homonnay
1/16/03 09:00:06 AM
CSO