CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22-078

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	October 17, 2007
To:	Mary Parks, MD Director, Division of Metablism and Endocrinology Products
Thru:	Kellie Taylor, PharmD, Acting Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Errors and Technical Support
From:	Judy Park, PharmD, Safety Evaluator Division of Medication Errors and Technical Support
Subject:	Labeling Review for Simcor
Drug Name(s):	Simcor (Niacin Extended-Release/Simvastatin) Tablets 500 mg/20 mg, 750 mg/20 mg, and 1000 mg/20 mg
Application Type/Number:	NDA 22-078
Applicant/sponsor:	Abbott
OSE RCM #:	2007-1512

1 INTRODUCTION

This memorandum is in response to a request from your Division for a review of the labels and labeling for Simcor (Niacin Extended-Release/Simvastatin). DMETS found the name, Simcor, acceptable in OSE review #06-0175 dated January 12, 2007. On April 17, 2007, the sponsor submitted the container labels and carton and insert labeling for review and comment.

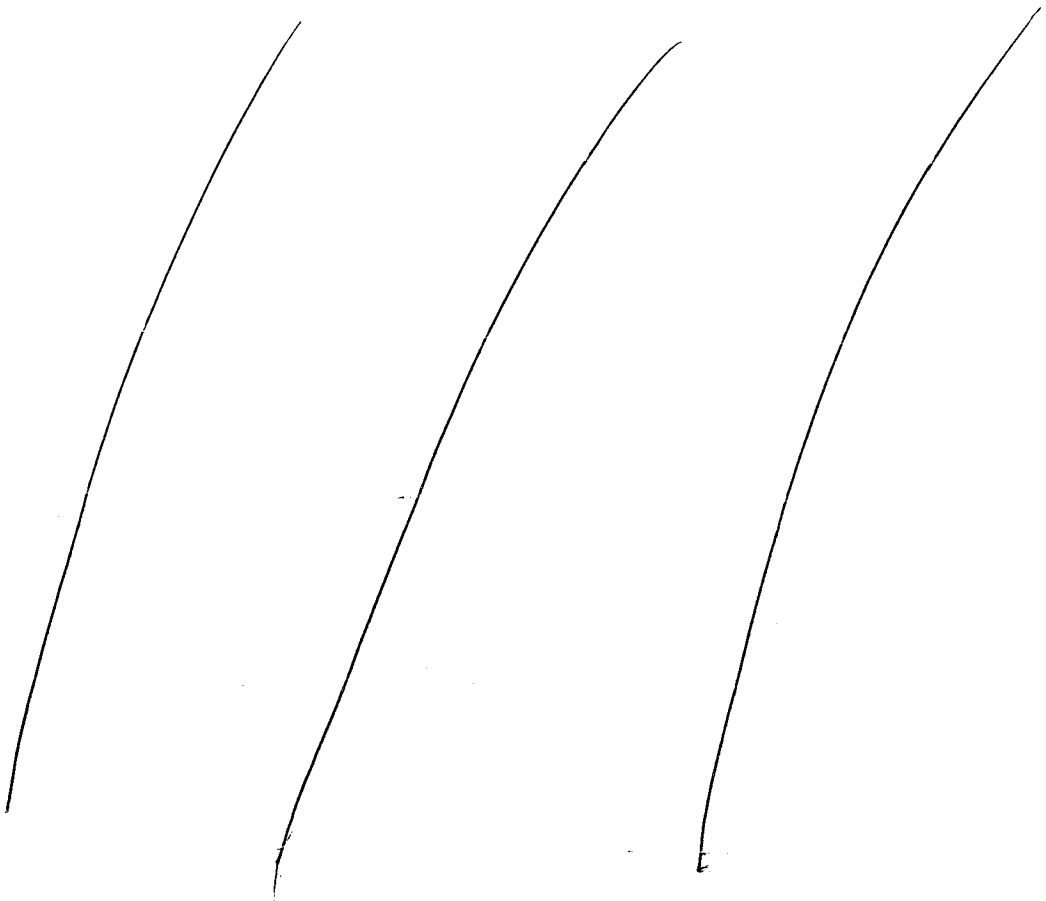
1.1 PRODUCT LABELING

Simcor is a fixed dose combination of two approved products, extended-release Niacin and Simvastatin. Simcor is indicated for the treatment of dyslipidemia. The usual dose is one tablet by mouth once daily and the dosage range is 500 mg/20 mg to 2000 mg/40 mg per day. Simcor will be available in three fixed-dose combinations of extended-release Niacin and Simvastatin: 500 mg/20 mg, 750 mg/20 mg, and 1000 mg/20 mg.

2 MATERIAL REVIEWED

DMETS reviewed the sample and trade container labels, sample carton labeling, patient information leaflet, and insert labeling for Simcor submitted on April 17, 2007.

3 DISCUSSION

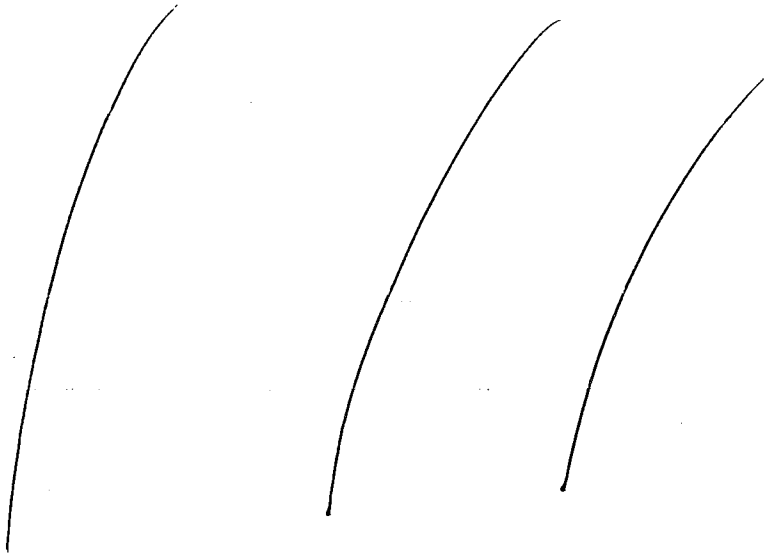


1 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process



DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. Please copy DMETS on any communication to the sponsor with regard to this review. Please also note that the proposed proprietary name, Simcor, must be re-evaluated by DMETS within 90 days of the PDUFA date. If you have further questions or need clarifications, please contact Cheryl Campbell, OSE project manager, at 301-796-0723.

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

/s/

Judy Park
10/17/2007 03:38:02 PM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
10/17/2007 04:05:31 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
10/17/2007 04:41:25 PM
DRUG SAFETY OFFICE REVIEWER

9/20/07

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	September 20, 2007
To:	Iffat Chowdhury, MD Medical Officer Division of Metabolism and Endocrinology Products Office of New Drugs
Thru:	Solomon Iyasu, MD, MPH Director Division of Surveillance, Research and Communication Support Office of Surveillance and Epidemiology
From:	Vicky Borders-Hemphill, Pharm.D., LCDR USPHS Drug Use Analyst Division of Surveillance, Research, and Communication Support Office of Surveillance and Epidemiology
Subject:	Concurrency Analysis VOCON: Zocor®/simvastatin concurrency with Niaspan® by strength
Drug Name(s):	Zocor®/simvastatin, Niaspan®, Simcor (Niacin ER/Simvastatin tablet)
Application Type/Number:	NDA 22-078
Applicant/sponsor:	Abbott Laboratories
OSE RCM #:	2007-1782

This document contains proprietary drug use data obtained by FDA under contract. The drug use data/information cannot be released to the public/non-FDA personnel without contractor approval obtained through the FDA/CDER Office of Surveillance and Epidemiology.

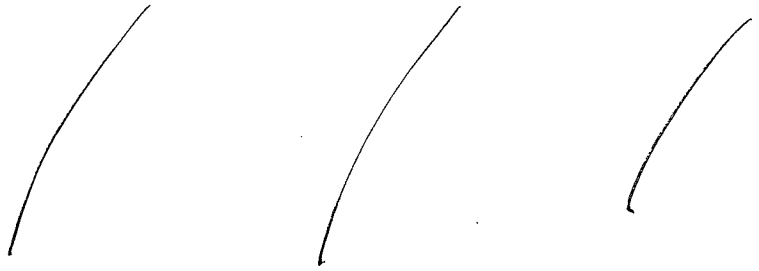
CONTENTS

EXECUTIVE SUMMARY

The Division of Metabolism and Endocrinology Products (DMEP) is reviewing an NDA (22-078) for a combination product containing niacin extended-release with simvastatin. DMEP requested a concurrency analysis providing Zocor® (simvastatin) use with Niaspan® by strength.

We examined the annual number of patients who filled a prescription for all approved strengths of brand and generic simvastatin concurrent with Niaspan® during the years 2002-2006. We utilized Verispan, Vector One®: Concurrency (VOCON) tool and conducted a concurrency analysis of Verispan's longitudinal prescription data for the years 2002-2006.

Please note. Data from VOCON are unprojected patient counts and may not be generalizable to all US patients.



1 INTRODUCTION

The Division of Metabolism and Endocrinology Products (DMEP) is reviewing an application submitted by Abbott Laboratories for Simcor® (niacin extended-release and simvastatin) 500 mg/20 mg, 750 mg/20 mg, and 1000 mg/ 20mg tablets in April 2007, under NDA 22-078, for the treatment of primary hypercholesterolemia, mixed dyslipidemia, and hypertriglyceridemia. DMEP requested a concurrency analysis providing simvastatin use with Niaspan®.

2 METHODS AND MATERIALS

2.1 INTRODUCTION

Using the currently available data resources, this review describes the concurrency between both brand and generic forms of simvastatin and the brand Niaspan®. Proprietary drug use databases licensed by the Agency were used to conduct this analysis.

2.2 DATA SOURCES USED

Utilizing the VOCON tool, we queried for concurrent use of all approved strengths of both brand and generic forms of simvastatin (20 mg, 40 mg, 80 mg) with the brand Niaspan®. An episode of concurrency is identified when a prescription in the Base group (simvastatin by strength) is dispensed on the same day as a prescription in the Concurrent group (Niaspan® by strength). Same day fill concurrency method was used to rule out therapeutic switching during the analysis period and to obtain the highest percentage of concurrency. Same day fill concurrency method does not allow for concurrency that occurs when patients are non-compliant or fill a prescription late. The days supply is calculated by adding the number of *therapy days* to the time of

prescription dispensing. The number of *therapy days* is estimated by dividing the number of tablets or capsules dispensed by the number of tablets or capsules consumed per day.

2.3 PRODUCTS INCLUDED

Forty-five sets of reports were generated from concurrency scenarios that were set up using the same day fill concurrency method. Analyses included five calendar years from 2002 through 2006. Data were analyzed for concurrency between each approved strength of both brand and generic forms of simvastatin (20 mg, 40 mg, 80 mg) with each approved strength of the brand Niaspan® (500 mg, 750 mg, 1000 mg).

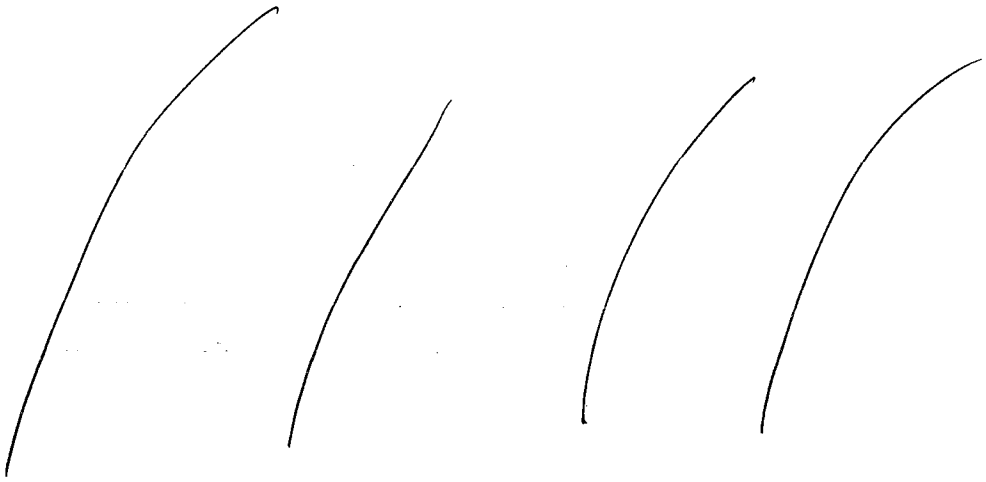
3 RESULTS

Table 1 (***see Appendix 2***) shows the overall concurrency between simvastatin and Niaspan® by year from 2002 through 2006. Tables 2-6 show the concurrency between each approved strength of both brand and generic forms of simvastatin (20 mg, 40 mg, 80 mg) with each approved strength of the brand Niaspan® (500 mg, 750 mg, 1000 mg) per year.

4 DISCUSSION

DMEP is currently reviewing an application for a product containing 20 mg of simvastatin combined with 500 mg, 750 mg, or 1000 mg of extended release niacin. Simvastatin is an HMG CoA reductase inhibitor, shown to be comparatively very efficacious in lowering LDL cholesterol levels and slightly elevating HDL cholesterol levels. Niacin, in smaller doses, very effectively elevates HDL cholesterol levels and lowers triglyceride levels. Niacin lowers LDL-cholesterol levels also, however, most effectively at doses greater than 2 grams per day. Niacin, at higher doses, is generally not well tolerated and is often used in combination with other cholesterol lowering agents to effectively lower LDL cholesterol. The National Cholesterol Education Program ATP III guideline recommends niacin as a therapeutic option for higher-risk persons with atherogenic dyslipidemia; being used as a single agent for those who do not have a substantial increase in LDL levels and in combination with other cholesterol lowering drugs in higher risk persons with atherogenic dyslipidemia with elevated LDL-levels.[1] Niaspan®, the only commercially available extended release niacin, was selected as a product for review.

[1] National Cholesterol Education Program. National Heart, Lung, and Blood Institute. National Institutes of Health. The Third Report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication No. 02-5215. September 2002.



5 CONCLUSIONS

Based on this analysis of a sample of patients, from 2002 through 2006, simvastatin 20 mg has a very low percentage of concurrency (less than — with all strengths of Niaspan®.

CONCURRENCE

Laura Governale, Pharm D., MBA.
Team Leader
Division of Surveillance, Research, and
Communication Support (DSRCS)

Solomon Iyasu, M D, MPH
Director
Division of Surveillance, Research, and
Communication Support (DSRCS)

APPENDICES

APPENDIX 1: DATABASE DESCRIPTIONS

Verispan, LLC: Vector One®: Concurrency (VOCON)

VOCON is an online concurrency analysis tool for the longitudinal prescription drug use database. It is sourced from Verispan's Vector One® database which receives over 1.8 billion prescription claims annually (approximately one-half the total U.S. volume) and represents over 150 million unique patients. VOCON allows users to measure and evaluate concurrent drug therapy usage in unique patients during a selected time period. VOCON provides **unprojected** patients counts; nationwide projections are not available.

---

[2] IMS Health, IMS Nationals Sales Perspectives™, Data extracted 8-10-2007. File: 0708nias.dvr

APPENDIX 2. TABLES

Table 1. Overall Years 2002-2006
VOCON concurrency Scenario Report: Total Number of Patients on Concurrent Therapy with Simvastatin (Zocor) and Niaspan overall during years **2002 through 2006**

Year	Patients (Simvastatin)	**Avg Patient Days Supply (Base)**	Patients (Niaspan)	Avg Patient Days Supply (Niaspan)	Total Patients (in Simvastatin OR Niaspan Group)	Total Patients (in Simvastatin AND Niaspan Groups)	Concurrent Patients	**% Concurrent of base**	Avg Concurrent Days	TRx (Simvastatin + Niaspan Groups)	TRx % (Simvastatin)	TRx % (Niaspan)
2002												
2003												
2004												
2005												
2006												

APPEARS THIS WAY
ON ORIGINAL

Table 2. Year 2002

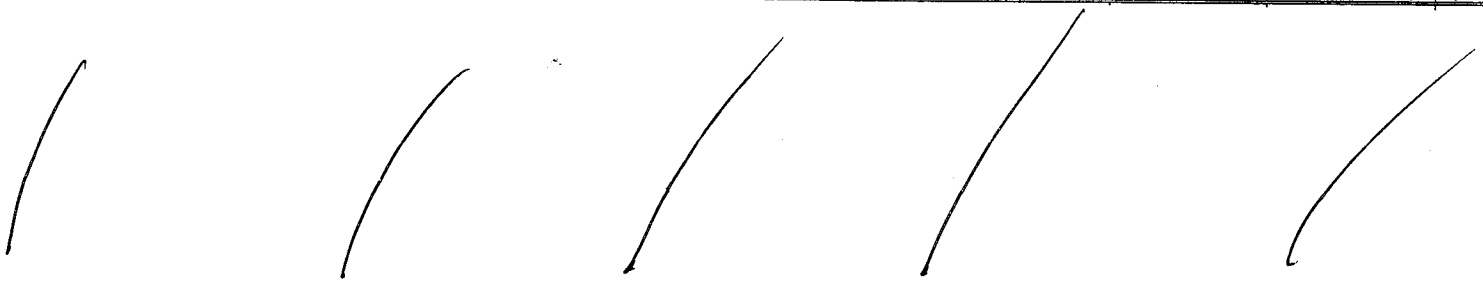
VOCON concurrency Scenario Report: Total Number of Patients on Concurrent Therapy with Simvastatin (Zocor) and Niaspan by strength during year **2002**

Combination (Simvastatin/ Niaspan)	Patients (Simvastatin)	**Avg Patient Days Supply (Base)**	Patients (Niaspan)	Avg Patient Days Supply (Niaspan)	Total Patients (in Simvastatin OR Niaspan Group)	Total Patients (in Simvastatin AND Niaspan Groups)	Concurrent Patients	**% Concurrent of base**	Avg Concurrent Days	TRx (Simvastatin + Niaspan Groups)	TRx % (Simvastatin)	TRx % (Niaspan)
20/500												
20/750												
20/1000												
40/500												
40/750												
40/1000												
80/500												
80/750												
80/1000												

APPEARS THIS WAY
ON ORIGINAL

Table 3. Year 2003
VOCON concurrency Scenario Report: Total Number of Patients on Concurrent Therapy with Simvastatin (Zocor) and Niaspan by strength during year **2003**

Combination (Simvastatin/ Niaspan)	Patients (Simvastatin)	**Avg Patient Days Supply (Base)**	Patients (Niaspan)	Avg Patient Days Supply (Niaspan)	Total Patients (in Simvastatin OR Niaspan Group)	Total Patients (in Simvastatin AND Niaspan Groups)	Concurrent Patients	**% Concurrent of base**	Avg Concurrent Days	TRx (Simvastatin + Niaspan Groups)	TRx % (Simvastatin)	TRx % (Niaspan)
20/500												
20/750												
20/1000												
40/500												
40/750												
40/1000												
80/500												
80/750												
80/1000												



APPEARS THIS WAY
ON ORIGINAL

Table 4. Year 2004
VOCON concurrency Scenario Report: Total Number of Patients on Concurrent Therapy with Simvastatin (Zocor) and Niaspan by strength during year **2004**

Combination (Simvastatin/ Niaspan)	Patients (Simvastatin)	**Avg Patient Days Supply (Base)**	Patients (Niaspan)	Avg Patient Days Supply (Niaspan)	Total Patients (in Simvastatin OR Niaspan Group)	Total Patients (in Simvastatin AND Niaspan Groups)	Concurrent Patients	**% Concurrent of base**	Avg Concurrent Days	TRx (Simvastatin + Niaspan Groups)	TRx % (Simvastatin)	TRx % (Niaspan)
20/500												
20/750												
20/1000												
40/500												
40/750												
40/1000												
80/500												
80/750												
80/1000												

APPEARS THIS WAY
ON ORIGINAL

Table 5. Year 2005

VOCON concurrency Scenario Report: Total Number of Patients on Concurrent Therapy with Simvastatin (Zocor) and Niaspan by strength during year **2005**

Combination (Simvastatin/ Niaspan)	Patients (Simvastatin)	**Avg Patient Days Supply (Base)**	Patients (Niaspan)	Avg Patient Days Supply (Niaspan)	Total Patients (in Simvastatin OR Niaspan Group)	Total Patients (in Simvastatin AND Niaspan Groups)	Concurrent Patients	**% Concurrent of base**	Avg Concurrent Days	TRx (Simvastatin + Niaspan Groups)	TRx % (Simvastatin)	TRx % (Niaspan)
20/500												
20/750												
20/1000												
40/500												
40/750												
40/1000												
80/500												
80/750												
80/1000												

APPEARS THIS WAY
ON ORIGINAL

Table 6. Year 2006

VOCON concurrency Scenario Report: Total Number of Patients on Concurrent Therapy with Simvastatin (Zocor) and Niaspan by strength during year **2006**

Combination (Simvastatin/ Niaspan)	Patients (Simvastatin)	**Avg Patient Days Supply (Base)**	Patients (Niaspan)	Avg Patient Days Supply (Niaspan)	Total Patients (in Simvastatin OR Niaspan Group)	Total Patients (in Simvastatin AND Niaspan Groups)	Concurrent Patients	**% Concurrent of base**	Avg Concurrent Days	TRx (Simvastatin + Niaspan Groups)	TRx % (Simvastatin)	TRx % (Niaspan)
20/500												
20/750												
20/1000												
40/500												
40/750												
40/1000												
80/500												
80/750												
80/1000												

APPEARS THIS WAY
ON ORIGINAL

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

/s/

Vicky Borders-Hemphill
9/20/2007 11:16:57 AM
DRUG SAFETY OFFICE REVIEWER

Solomon Iyasu
9/20/2007 12:39:43 PM
MEDICAL OFFICER