

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

18-612/S-050

20-066/S-031

Trade Name: Nicorette

Generic Name: nicotine polacrilex gum, 2mg and 4mg

Sponsor: GlaxoSmithKline Consumer Healthcare, L.P.

Approval Date: June 13, 2008

Purpose: The nonprescription marketing of a new White Ice Mint flavor of 2mg and 4mg gum with associated packaging and labeling.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

18-612/S-050 & 20-066/S-031

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**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
18-612/S-050 & 20-066/S-031

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-612/S-050
NDA 20-066/S-031

GlaxoSmithKline Consumer Healthcare, L.P.
Attention: Marissa M. Fletcher, Ph.D.
Manager, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Dr. Fletcher:

Please refer to your supplemental new drug applications for NDA 18-612 dated February 13, 2008, received February 13, 2008, and NDA 20-066 dated February 14, 2008 received February 14, 2008, submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act for:

NDA Number	Name	Dosage Form
18-612/S-050	Nicorette	2 mg, nicotine polacrilex gum
20-066/S-031	Nicorette	4 mg, nicotine polacrilex gum

We also acknowledge receipt of your submissions dated March 21, and June 10, 2008 to both NDAs.

This supplemental new drug application provides for the nonprescription marketing of a new White Ice Mint flavor of 2 mg and 4 mg gum with associated packaging and labeling.

We have completed our review of these applications. 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 (10-count blister card, 20-, 100- and 160-count carton labels and users guide for the 2 and 4 mg strengths), and must be formatted in accordance with the requirements of 21 CFR 201.66, where applicable.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions **"FPL for approved supplement NDA 18-612/S-050 and NDA 20-066/S-031."** Approval of these submissions by FDA is not required before the labeling is used.

We remind you that the word "New" must be removed from the label and labeling, wherever it appears, after the first six months of marketing.

NDA18-612/S-050
NDA 20-066/S-031
Page 2

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

In addition, we remind you that the statement of identity phrase "STOP SMOKING AID" on the principal display panel should be capitalized at the time of next printing of the label or within 180 days, whichever is sooner.

Please submit one market package of the drug product when it is available.

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 Mary Lewis, Regulatory Project Manager, at (301) 796-0941.

Sincerely,

{See appended electronic signature page}

Joel Schiffenbauer, M.D.
Deputy Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
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/

Joel Schiffenbauer
6/13/2008 09:57:13 AM

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
18-612/S-050 & 20-066/S-031

LABELING

[illegible]

OPEN HERE

818317

818317

THEFT SURVEILLANCE TAG AREA

PLACE
ANTI-THEFT
STICKER
HERE**Drug Facts (continued)****Other information**

each piece contains:
 calcium 94mg, sodium 11mg
 • store at 20°-25°C (68°-77°F)
 • protect from light

Inactive ingredients saccharin,
 potassium, carnauba wax, edible ink, flavor, gum
 base, hypromellose, magnesium oxide, menthol,
 peppermint oil, polyacrylate 60, sodium
 bicarbonate, sodium carbonate, starch, sucralose,
 titanium dioxide, xylitol

Questions or comments?

call toll-free 1-800-411-4746 (English/Spanish)
 weekdays (9:00 am - 4:30 pm ET)

Drug Facts**Active ingredient (in each chewing piece)**

Nicotine polacrilex (equal to 2mg nicotine)

Purpose

Stop smoking aid

Use - reduces withdrawal symptoms, including nicotine craving, associated with quitting smoking**Warnings**

If you are pregnant or breast-feeding, only use this medicine on the advice of your health care provider.
 Smoking can seriously harm your child. Try to stop smoking without using any nicotine replacement medicine. This
 medicine is believed to be safer than smoking. However, the risks to your child from this medicine are not fully known.

Do not use

- if you continue to smoke, chew tobacco, use snuff, or use a nicotine patch or other nicotine containing products

Ask a doctor before use if you have

- a sodium-restricted diet
- heart disease, recent heart attack, or irregular heartbeat. Nicotine can increase your heart rate.
- high blood pressure not controlled with medication. Nicotine can increase blood pressure.
- stomach ulcer or diabetes

Ask a doctor or pharmacist before use if you are

- using a non-nicotine stop smoking drug
- taking prescription medicine for depression or asthma. Your prescription dose may need to be adjusted.

Stop use and ask a doctor if

- mouth, teeth or jaw problems occur
- irregular heartbeat or palpitations occur
- you get symptoms of nicotine overdose such as nausea, vomiting, dizziness, diarrhea, weakness and rapid heartbeat

Keep out of reach of children and pets. Pieces of nicotine gum may have enough nicotine to make children and
 pets sick. Wrap used pieces of gum in paper and throw away in the trash. In case of overdose, get medical help or
 contact a Poison Control Center right away.

Directions

- If you are under 18 years of age, ask a doctor before use
- before using this product, read the enclosed User's Guide for complete directions and other important information
- stop smoking completely when you begin using the gum
- if you smoke 25 or more cigarettes a day, use 4mg nicotine gum
- if you smoke less than 25 cigarettes a day, use according to the following 12 week schedule:

Weeks 1 to 6	Weeks 7 to 9	Weeks 10 to 12
1 piece every 1 to 2 hours	1 piece every 2 to 4 hours	1 piece every 4 to 8 hours

- nicotine gum is a medicine and must be used a certain way to get the best results
- chew the gum slowly until it tingles. Then park it between your cheek and gum. When the tingle is gone, begin
 chewing again, until the tingle returns.
- repeat this process until most of the tingle is gone (about 30 minutes)
- do not eat or drink for 15 minutes before chewing the nicotine gum, or while chewing a piece
- to improve your chances of quitting, use at least 9 pieces per day for the first 6 weeks
- if you experience strong or frequent cravings, you may use a second piece within the hour. However, do not
 continuously use one piece after another since this may cause you hiccups, heartburn, nausea or other side effects.
- do not use more than 24 pieces a day
- it is important to complete treatment. Stop using the nicotine gum at the end of 12 weeks. If you still feel the need
 to use nicotine gum, talk to your doctor.

EAS Tagged

44



Nicorette®
 White Ice™ Mint Gum

- not for sale to those under 18 years of age
- proof of age required
- not for sale in vending machines or from any source where proof of age cannot be verified

This product is protected in sealed blisters. Do not use if individual blisters or printed backings are broken, open, or torn.

Distributed by:
 GlaxoSmithKline Consumer Healthcare, LP,
 Moon Township, PA 15108
 Made in Sweden

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304820A

For more information and for a FREE
 Individualized stop smoking program, please visit
www.Nicorette.com or see inside for more details.

Free Audio CD upon request. See inside.
 Includes Carrying Case

Important: Nicotine replacement therapy (NRT) is not a cure for nicotine addiction. It is only a temporary aid to help you quit smoking. You must be a legal U.S. resident, 18 years of age or older, and have smoked at least one cigarette per day for the past 12 weeks. Do not use if you are pregnant, breastfeeding, or have a heart condition, high blood pressure, or are taking certain medications. For complete terms and conditions, visit www.nicorette.com.

QUIT REWARDS

Nicorette®
 White Ice™ Mint Gum

100 PIECES, 2mg EACH

Coated
 for Intense Flavor
 White Ice™ Mint Gum

Nicorette
 polacrilex gum, 2mg • stop-smoking aid

QUIT REWARDS
 Earn \$170 over \$50 in coupons and rewards
 by completing and returning
 the Nicorette Quit Rewards Card

NEW FLAVOR
 100 PIECES, 2mg EACH

OPEN HERE

OPEN HERE

NICORETTE® 2mg
nicotine polacrilex
White Ice™ Mint
Distributed by:
GlaxoSmithKline
Moon Twp, PA 15108
1 piece
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NICORETTE® 2mg
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White Ice™ Mint
Distributed by:
GlaxoSmithKline
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White Ice™ Mint
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Moon Twp, PA 15108
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NICORETTE® 2mg
nicotine polacrilex
White Ice™ Mint
Distributed by:
GlaxoSmithKline
Moon Twp, PA 15108
1 piece
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NICORETTE® 2mg White Ice™ Mint 10 pieces
Chew Activated Release. Keep out of reach of children.

58239XA

NICORETTE® 4mg nicotine polacrilex White Ice™ Mint Distributed by: GlaxoSmithKline Moon Twp, PA 15108 1 piece 00000 00/0000	NICORETTE® 4mg nicotine polacrilex White Ice™ Mint Distributed by: GlaxoSmithKline Moon Twp, PA 15108 1 piece 00000 00/0000
NICORETTE® 4mg nicotine polacrilex White Ice™ Mint Distributed by: GlaxoSmithKline Moon Twp, PA 15108 1 piece 00000 00/0000	NICORETTE® 4mg nicotine polacrilex White Ice™ Mint Distributed by: GlaxoSmithKline Moon Twp, PA 15108 1 piece 00000 00/0000
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NICORETTE® 4mg White Ice™ Mint 10 pieces
Chew Activated Release® Keep out of reach of children

58233XA

Nicorette®

nicotine polacrilex gum
2mg and 4mg User's Guide



HOW TO USE NICORETTE TO HELP YOU QUIT SMOKING.

Copyright ©2006 GlaxoSmithKline Consumer Healthcare, L.P.



(See insert)

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KEYS TO SUCCESS.

- 1) You must really want to quit smoking for **Nicorette**® to help you.
- 2) You can greatly increase your chances for success by using at least 9 to 12 pieces every day when you start using **Nicorette**. See page 12.
- 3) You should continue to use **Nicorette** as explained in this User's Guide for 12 full weeks.
- 4) **Nicorette** works best when used together with a support program — See page 3 for details.
- 5) If you have trouble using **Nicorette**, ask your doctor or pharmacist or call GlaxoSmithKline at 1-800-419-4766 weekdays (10:00 am - 4:30 pm EST.)
- 6) To request a free audio CD containing tips to help make quitting easier, call the toll free number listed above. (ONE CD PER CUSTOMER)



SO YOU DECIDED TO QUIT.

Congratulations.

Your decision to stop smoking is an important one. That's why you've made the right choice in choosing **Nicorette** gum.

Your own chances of quitting smoking depend on how much you want to quit, how strongly you are addicted to tobacco, and how closely you follow a quitting program like the one that comes with **Nicorette**.

QUITTING SMOKING IS HARD!

If you've tried to quit before and haven't succeeded, don't be discouraged! Quitting isn't easy. It takes time, and most people try a few times before they are successful. The important thing is to try again until you succeed. This User's Guide will give you support as you become a non-smoker. It will answer common questions about **Nicorette** and give tips to help you stop smoking, and should be referred to often.

WHERE TO GET HELP. You are more likely to stop smoking by using **Nicorette** with a support program that helps you break your smoking habit. There may be support groups in your area for people trying to quit. Call your local chapter of the American Lung Association, American Cancer Society or American Heart Association for further information. Toll free phone numbers are printed on the Wallet Card on the back cover of this User's Guide.

If you find you cannot stop smoking or if you start smoking again after using **Nicorette**, remember breaking this addiction doesn't happen overnight. You may want to talk to a health care professional who can help you improve your chances of quitting the next time you try **Nicorette** or another method.

LET'S GET ORGANIZED. Your reason for quitting may be a combination of concerns about health, the effect of smoking on your appearance, and pressure from your family

and friends to stop smoking. Or maybe you're concerned about the dangerous effect of second-hand smoke on the people you care about. All of these are good reasons. You probably have others. Decide your most important reasons, and write them down on the wallet card inside the back cover of this User's Guide. Carry this card with you. In difficult moments, when you want to smoke, the card will remind you why you are quitting.

WHAT YOU'RE UP AGAINST. Smoking is addictive in two ways. Your need for nicotine has become both physical and mental. You must overcome both addictions to stop smoking. So while **Nicorette** will lessen your body's physical addiction to nicotine, you've got to want to quit smoking to overcome the mental dependence on cigarettes. Once you've decided that you're going to quit, it's time to get started. But first, there are some important warnings you should consider.

SOME IMPORTANT WARNINGS. This product is only for those who want to stop smoking. **If you are pregnant or breast-feeding, only use this medicine on the advice of your health care provider.** Smoking can seriously harm your child. Try to stop smoking without using any nicotine replacement medicine. This medicine is believed to be safer than smoking. However, the risks to your child from this medicine are not fully known.

Do not use

- if you continue to smoke, chew tobacco, use snuff, or use a nicotine patch or other nicotine containing products.

Ask a doctor before use if you have

- a sodium-restricted diet
- heart disease, recent heart attack, or irregular heartbeat. Nicotine can increase your heart rate.
- high blood pressure not controlled with medication. Nicotine can increase your blood pressure.
- stomach ulcer or diabetes

Ask a doctor or pharmacist before use if you are

- using a non-nicotine stop smoking drug
- taking a prescription medicine for depression or asthma. Your prescription dose may need to be adjusted.

Stop use and ask a doctor if

- mouth, teeth or jaw problems occur
- irregular heartbeat or palpitations occur
- you get symptoms of nicotine overdose such as nausea, vomiting, dizziness, diarrhea, weakness and rapid heartbeat

Keep out of reach of children and pets.

Pieces of nicotine gum may have enough nicotine to make children and pets sick. Wrap used pieces of gum in paper and throw away in the trash. In case of overdose, get medical help or contact a Poison Control Center right away.

LET'S GET STARTED. Becoming a non-smoker starts today. First, check that you bought the right starting dose. **If you smoke 25 or more cigarettes a day, use 4 mg nicotine gum. If you smoke less than 25 cigarettes a day, use 2 mg**

nicotine gum. Next, read through the entire User's Guide carefully. Then, set your personalized quitting schedule. Take out a calendar that you can use to track your progress, and identify four dates, using the stickers in the center of this User's Guide:

STEP 1. (Weeks 1-6). Your quit date (and the day you'll start using Nicorette gum). Choose your quit date (it should be soon). This is the day you will quit smoking cigarettes entirely and begin using Nicorette to satisfy your cravings for nicotine. For the first six weeks, you'll use a piece of

Nicorette every hour or two. Be sure to follow the directions starting on pages 10 and 12. Place the Step 1 stickers on this date.

STEP 2. (Weeks 7 to 9). The day you'll start reducing your use of Nicorette.

After six weeks, you'll begin gradually reducing your Nicorette usage to one piece every two to four hours. Place the Step 2 sticker on this date (the first day of week seven).

STEP 3. (Weeks 10-12). The day you'll further reduce your use of Nicorette.

Nine weeks after you begin using **Nicorette**, you will further reduce your nicotine intake by using one piece every four to eight hours. Place the Step 3 sticker on this date (the first day of week ten). For the next three weeks, you'll use a piece of **Nicorette** every four to eight hours.

End of treatment: The day you'll complete Nicorette therapy.

Nicorette should not be used for longer than twelve weeks. Identify the date thirteen weeks after the date you chose in Step 1, and place the "EX-SMOKER" sticker on your calendar.

PLAN AHEAD. Because smoking is an addiction, it is not easy to stop. After you've given up cigarettes, you will still have a strong urge to smoke. Plan ahead NOW for these times, so you're not defeated in a moment of weakness. The following tips may help:

- Keep the phone numbers of supportive friends and family members handy.
- Keep a record of your quitting process. Track the number of **Nicorette** pieces you use each day, and whether you feel a craving for cigarettes. In the event that

you slip, immediately stop smoking and resume your quit attempt with the **Nicorette** program.

- Put together an Emergency Kit that includes items that will help take your mind off occasional urges to smoke. Include cinnamon gum or lemon drops to suck on, a relaxing cassette tape, and something for your hands to play with, like a smooth rock, rubber band, or small metal balls.
- Set aside some small rewards, like a new magazine or a gift certificate from your favorite store, which you'll "give" yourself after passing difficult hurdles.
- Think now about the times when you most often want a cigarette, and then plan what else you might do instead of smoking. For instance, you might plan to take your coffee break in a new location, or take a walk right after dinner, so you won't be tempted to smoke.

HOW NICORETTE GUM WORKS. Nicorette's sugar-free chewing pieces provide nicotine to your system – they work as a temporary aid to help you quit smoking by reducing nicotine withdrawal symptoms. Nicorette provides a lower level of nicotine to your blood than cigarettes, and allows you to gradually do away with your body's need for nicotine. Because Nicorette does not contain the tar or carbon monoxide of cigarette smoke, it does not have the same health dangers as tobacco. However, it still

delivers nicotine, the addictive part of cigarette smoke. Nicotine can cause side effects such as headache, nausea, upset stomach, and dizziness.

HOW TO USE NICORETTE GUM. If you are under 18 years of age, ask a doctor before use. Before you can use Nicorette correctly, you have to practice! That sounds silly, but it isn't. Nicorette isn't like ordinary chewing gum. It's a medicine, and must be chewed a certain way to work right. Chewed like ordinary gum, Nicorette won't work well and

can cause side effects. An overdose can occur if you chew more than one piece of **Nicorette** at the same time, or if you chew many pieces one after another. Read all the following instructions before using **Nicorette**. Refer to them often to make sure you're using **Nicorette** gum correctly. If you chew too fast, or do not chew correctly, you may get hiccups, heartburn, or other stomach problems. Don't eat or drink for 15 minutes before using **Nicorette**, or while chewing a piece. The effectiveness of **Nicorette** may be reduced by some foods and drinks, such as

coffee, juices, wine or soft drinks.

- 1) Stop smoking completely before you start using **Nicorette**.
- 2) To reduce craving and other withdrawal symptoms, use **Nicorette** according to the dosage schedule on page 12.
- 3) Chew each **Nicorette** piece very slowly several times.
- 4) Stop chewing when you notice a peppery taste, or a slight tingling in your mouth. (This usually happens after about 15 chews, but may vary from person to person.)

- 5) "PARK" the **Nicorette** piece between your cheek and gum, and leave it there.
- 6) When the peppery taste or tingle is almost gone (in about a minute), start to chew a few times slowly again. When the taste or tingle returns, stop again.
- 7) Park the **Nicorette** piece again (in a different place in your mouth).
- 8) Repeat steps 3 to 7 (chew, chew, park) until most of the nicotine is gone from the **Nicorette** piece (usually happens in about half an hour; the peppery taste or tingle won't return.)

- 9) Wrap the used **Nicorette** piece in paper and throw away in the trash.

The following chart lists the recommended usage schedule for Nicorette:		
Weeks 1 to 6	Weeks 7 to 9	Weeks 10 to 12
1 piece every 1 to 2 hours	1 piece every 2 to 4 hours	1 piece every 4 to 8 hours
DO NOT USE MORE THAN 24 PIECES PER DAY.		

To improve your chances of quitting, use at least 9 pieces of **Nicorette** a day. If you experience strong or frequent cravings, you may use a second piece within the hour. However, do not continuously use one



To Enroll Call Now

or enroll online at



Having a Plan Will Help You Quit



Nicorette
INDIVIDUALIZED STOP
SMOKING PROGRAM
**COMMITTED
QUITTERS™**

*is a FREE custom-tailored
plan to help you break your
psychological addiction to
smoking — while NICORETTE® fights
the physical addiction. To get your
plan, call toll free 1-800-770-0708 or visit us
on the Web at www.committedquitters.com.*

CALL:

Provide your **Committed Quitters®** personal code (the personal code is located within the **Committed Quitters®** portion of this User's Guide). You will be asked a few questions by a plan specialist to understand YOU and YOUR specific needs.

CALL:

In a few days, you will receive your custom-tailored stop smoking plan. You will continue to receive personal, custom-tailored support — six times during the next twelve weeks.

Your Plan Will Contain:

Week 1



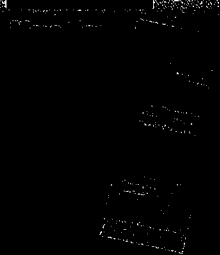
Week 2



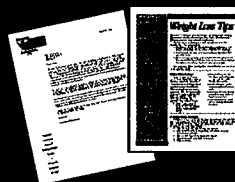
Week 3



Week 6



Week 9



Week 12



Materials are subject to change.

First Week:

**1. Control your physical
cravings for nicotine.**

Use enough — You can greatly increase your chances for success by using at least 9 to 12 pieces every day when you start using Nicorette.

**2. Get rid of all signs that you
ever smoked —**

ashtrays, matches and, of course, cigarettes.

3. Stay active.

Keep busy to take your mind off smoking.

4. Think positive!

The first week is the toughest. Remind yourself that it will get easier.

Use the sample of the Stop Smoking Plan (see next page) to get you through the first week until your materials arrive.

WEEK ONE

Remember to try one of the smoke-free
nicotine ways to keep your cravings under
control. Remember, only the nicotine
from the gum helps you quit.

CALENDAR

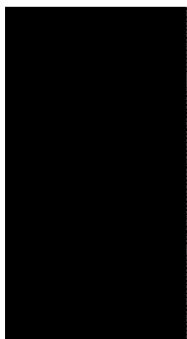
Day Pieces Chewed Planning: Plan ahead. Note events here that will tempt you to smoke, and how you will deal with them.

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____

TIPS

If you have gone back to smoking, call 1-800-770-0708 to order relapse information.

*Carry this calendar with you.



*The **Committed Quitters**® program is a
plan specifically individualized for you.*

**Call Between 7 am and 12 Midnight EST or enroll
online 24 hours a day. (ONE PLAN PER CUSTOMER)**

Nicorette, Committed Quitters and associated logo designs, and overall trade
dress designs are trademarks owned by or licensed to GlaxoSmithKline.

Read and follow label directions
©2006 GlaxoSmithKline

FOLD LINE

piece after another, since this may cause you hiccups, heartburn, nausea or other side effects.

HOW TO REDUCE YOUR NICORETTE USAGE.

The goal of using **Nicorette** is to slowly reduce your dependence on nicotine. The schedule for using **Nicorette** will help you reduce your nicotine craving gradually as you reduce and then stop your use of **Nicorette**. Here are some tips to help you cut back during each step and then stop using **Nicorette**:

- After a while, start chewing each **Nicorette** piece for only 10 to 15 minutes, instead of half an hour. Then, gradually begin to reduce the number of pieces used.
- Or, try chewing each piece for longer than half an hour, but reduce the number of pieces you use each day.
- Substitute ordinary chewing gum for some of the **Nicorette** pieces you would normally use. Increase the number of pieces of ordinary gum as you cut back on the **Nicorette** pieces.

- Check how well you've reduced your daily usage of **Nicorette** in Weeks 10 to 12. You should only be using about 3 to 5 pieces a day. Get ready to stop.

STOP USING NICORETTE AT THE END OF WEEK 12. The following tips may help you with stopping **Nicorette** Gum at the end of 12 weeks.

- Set a stop date.
- Use the same number of pieces of confectionery gum or mints as you were using **Nicorette** per day.

At the times when you have an urge to use **Nicorette**, use a strong flavored gum or mint such as cinnamon or peppermint.

- Reduce the number of pieces of gum or mints you use by one piece per day until you do not need to use any gum or mints.

Talk to your doctor if you:

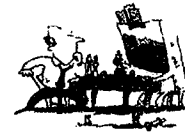
- still feel the need to use **Nicorette** at the end of week 12
- start using **Nicorette** again after stopping
- start smoking again

TIPS TO MAKE QUITTING EASIER. Within the first few weeks of giving up smoking, you may be tempted to smoke for pleasure, particularly after completing a difficult task, or at a party or bar. Here are some tips to help get you through the important first stages of becoming a non-smoker:

On Your Quit Date:

- Ask your family, friends and co-workers to support you in your efforts to stop smoking.

- Throw away all your cigarettes, matches, lighters, ashtrays, etc.
- Keep busy on your quit day. Exercise. Go to a movie. Take a walk. Get together with friends.
- Figure out how much money you'll save by not smoking. Most ex-smokers can save more than \$1,000 a year.
- Write down what you will do with the money you save.



- Know your high risk situations and plan ahead how you will deal with them.
- Keep **Nicorette** gum near your bed, so you'll be prepared for any nicotine cravings when you wake up in the morning.
- Visit your dentist and have your teeth cleaned to get rid of the tobacco stains.

Right after Quitting:

- During the first few days after you've stopped smoking, spend as much time as possible at places where smoking is not allowed.
- Drink large quantities of water and fruit juices.
- Try to avoid alcohol, coffee and other beverages you associate with smoking.
- Remember that temporary urges to smoke will pass, even if you don't smoke a cigarette.
- Keep your hands busy with something like a pencil or a paper clip.
- Find other activities which help you relax without cigarettes.
- Swim, jog, take a walk, play basketball.

- Don't worry too much about gaining weight. Watch what you eat, take time for daily exercise, and change your eating habits if you need to.
- Laughter helps. Watch or read something funny.



WHAT TO EXPECT. Your body is now coming back into balance. During the first few days after you

stop smoking, you might feel edgy and nervous and have trouble concentrating. You might get headaches, feel dizzy and a little out of sorts, feel sweaty or have stomach upsets. You might even have trouble sleeping at first. These are typical withdrawal symptoms that will go away with time. Your smoker's cough will get worse before it gets better. But don't worry, that's a good sign. Coughing helps clear the tar deposits out of your lungs.

After A Week Or Two.

By now you should be feeling more confident that you can handle those smoking urges. Many of your withdrawal symptoms have left by now, and you should be noticing some positive signs: less coughing, better breathing and an improved sense of taste and smell, to name a few.

After A Month.

You probably have the urge to smoke much less often now. But urges may still occur, and when they do, they are likely

to be powerful ones that come out of nowhere. Don't let them catch you off guard. Plan ahead for these difficult times. Concentrate on the ways non-smokers are more attractive than smokers. Their skin is less likely to wrinkle. Their teeth are whiter, cleaner. Their breath is fresher. Their hair and clothes smell better. That cough that seems to make even a laugh sound more like a rattle is a thing of the past. Their children and others around them are healthier, too.

What To Do About Relapse.

What should you do if you slip and start smoking again? The answer is simple. A lapse of one or two or even a few cigarettes has not spoiled your efforts! Discard your cigarettes, forgive yourself and try again. If you start smoking again, keep your box of **Nicorette** for your next quit attempt.

If you have taken up regular smoking again, don't be discouraged. Research shows that the best thing you can do is to try again. The important thing is to learn from your last attempt.

- Admit that you've slipped, but don't treat yourself as a failure.
- Try to identify the "trigger" that caused you to slip, and prepare a better plan for dealing with this problem next time.
- Talk positively to yourself – tell yourself that you have learned something from this experience.
- Make sure you used **Nicorette** gum correctly over the full 12 weeks to reduce your craving for nicotine.
- Remember that it takes practice to do

anything, and quitting smoking is no exception.

**WHEN THE
STRUGGLE
IS OVER.**

Once you've stopped smoking, take a second and pat yourself on your back. Now do it again.

You deserve it. Remember now why you decided to stop smoking in the first place. Look at your list of reasons. Read them again. And smile. Now think about all the money you are saving and what you'll do with it. All the non-smoking places you can go, and what you might do there. All

those years you may have added to your life, and what you'll do with them.

Remember that temptation may not be gone forever. However, the hard part is behind you so look forward with a positive attitude, and enjoy your new life as a non-smoker.

QUESTIONS & ANSWERS.

1. How will I feel when I stop smoking and start using Nicorette?

You'll need to prepare yourself for some nicotine withdrawal symptoms. These begin almost immediately after you stop

smoking, and are usually at their worst during the first three or four days. Understand that any of the following is possible:

- craving for cigarettes
- anxiety, irritability, restlessness, mood changes, nervousness
- drowsiness
- trouble concentrating
- increased appetite and weight gain
- headaches, muscular pain, constipation, fatigue.

Nicorette can help provide relief from withdrawal symptoms such as irritability and nervousness, as well as the craving for nicotine you used to satisfy by having a cigarette.

2. Is Nicorette just substituting one form of nicotine for another?

Nicorette does contain nicotine. The purpose of **Nicorette** is to provide you with enough nicotine to help control the physical withdrawal symptoms so you can deal with the mental aspects of quitting. During the 12 week program, you will gradually

reduce your nicotine intake by switching to fewer pieces each day. Remember, don't use **Nicorette** together with nicotine patches or other nicotine containing products.

3. Can I be hurt by using Nicorette?

For most adults, the amount of nicotine in the gum is less than from smoking. Some people will be sensitive to even this amount of nicotine and should not use this product without advice from their doctor (see page 5).

Because **Nicorette** is a gum-based product, chewing it can cause dental fillings to loosen and aggravate other mouth, tooth and jaw problems. **Nicorette** can also cause hiccups, heartburn and other stomach problems especially if chewed too quickly or not chewed correctly.

4. Will I gain weight?

Many people do tend to gain a few pounds the first 8-10 weeks after they stop smoking. This is a very small price to pay for the enormous gains that you will make in your overall health and attractiveness. If you

continue to gain weight after the first two months, try to analyze what you're doing differently. Reduce your fat intake, choose healthy snacks, and increase your physical activity to burn off the extra calories.

5. Is Nicorette more expensive than smoking?

The total cost of **Nicorette** for the twelve week program is about equal to what a person who smokes one and a half packs of cigarettes a day would spend on cigarettes for the same period of time.

Also, use of **Nicorette** is only a short-term cost, while the cost of smoking is a long-term cost, because of the health problems smoking causes.

6. What if I slip up?

Discard your cigarettes, forgive yourself and then get back on track. Don't consider yourself a failure or punish yourself. In fact, people who have already tried to quit are more likely to be successful the next time.

**GOOD
LUCK!**



**Recommended dosage
schedule for Nicorette:**

STEP 1	STEP 2	STEP 3
weeks 1 to 6 1 piece every 1 to 2 hours	weeks 7 to 9 1 piece every 2 to 4 hours	weeks 10 to 12 1 piece every 4 to 8 hours

**WALLET
CARD**

**My most important reasons
to quit smoking are:**

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WHERE TO CALL FOR HELP:

American Lung Association
1-800-536-4672

American Cancer Society
1-800-227-2345

American Heart Association
1-800-242-8721

**WALLET
CARD**

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

18-612/S-050 & 20-066/S-031

CHEMISTRY REVIEW(S)

OFFICE ON NEW DRUG QUALITY ASSESSMENT
DIVISION OF POST-MARKETING EVALUATION, BRANCH VIII
Review of Chemistry, Manufacturing, and Controls
for the Division of Non-prescription Products, HFD-560

NDA #: 18-612 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 04-JUN-2008
20-066

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
NDA 18-612/SCF-050	13-FEB-2008	13-FEB-2008	04-MAR-2008
NDA 20-066/SCF-031	13-FEB-2008	13-FEB-2008	04-MAR-2008
NDA 18-612/SCF-050 (BC)	21-MAR-2008	21-MAR-2008	21-MAR-2008
NDA 20-066/SCF-031 (BC)	21-MAR-2008	21-MAR-2008	21-MAR-2008

NAME & ADDRESS OF APPLICANT: GlaxoSmithKline
1500 Littleton Road
Parsippany, NJ 0704

Marissa M. Fletcher, Ph.D.
Manager, Regulatory Affairs
(973) 889-4443

DRUG PRODUCT NAME

Proprietary:

Nonproprietary/USAN:

Code Names/#'s:

Chemical Type/

Therapeutic Class:

Nicorette® Gum

Nicotine Polacrilex

(b) (4)

PHARMACOLOGICAL

CATEGORY/INDICATION: Reduces withdrawal symptoms, including nicotine craving, associated with quitting smoking.

DOSAGE FORM:

Gum, chewing, buccal

STRENGTHS:

2mg; 4mg

ROUTE OF ADMINISTRATION:

Oral

DISPENSED:

___ Rx X OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOL.WT:

Nicotine: 3-(1-Methyl-2-pyrrolidiny)pyridine; or β -Pyridyl- α -N-methyl pyrrolidine

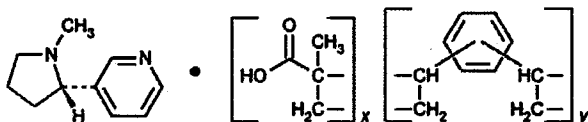
CAS No.: [54-11-5]

Molecular Formula: C₁₀H₁₄N₂

Molecular Weight: 162.23

**Nicorette® Original and Mint (nicotine polacrilex) Gums, 2mg and 4mg
GlaxoSmithKline**

Nicotine Polacrilex is a nicotine complex with a weak carboxylic cation-exchange resin prepared from methacrylic acid and divinylbenzene. It contains not less than 95.0% and not more than 115.0% of the labeled amount of nicotine, calculated on the anhydrous basis.



CAS No.:

[96055-45-7]

RELATED DOCUMENTS:

NDA 18-612/SCF-028, NDA 20-066/SCF-016; approved 25-SEP-2000

NDA 18-612/SCF-037, NDA 20-066/SCF-019; approved 18-JUN-2004

NDA 18-612/SCF-042, NDA 20-066/SCF-023; approved 02-DEC-2005

NDA 18-612/SCF-049, NDA 20-066/SCF-030; approved 26-JUN-2007

SUPPORTING DOCUMENTS:

DMF 3835, Type II, for Nicotine Polacrilex Gums, held by McNeil Consumer Healthcare, a Johnson & Johnson Co., Letter of Authorization dated 14-MAR-2008. [On December 21, 2006, former DMF holder Pfizer sold its consumer healthcare business (the manufacturer of Nicorette® Gum) to Johnson & Johnson.]

DMF 5757, Type II, for Nicotine Polacrilex Resin 20%, held by McNeil Consumer Healthcare, a Johnson & Johnson Co., Letter of Authorization dated 15-FEB-2008. [On December 21, 2006, former DMF holder Pfizer sold its consumer healthcare business (the manufacturer of Nicorette® Gum) to Johnson & Johnson.]

DMF 3831, Type II, Nicotine Polacrilex Gums Manufactured at Esbjerg, Denmark, held by McNeil Consumer Healthcare, a Johnson & Johnson Co., Letter of Authorization dated 24-JUL-2006. [On December 21, 2006, former DMF holder Pfizer sold its consumer healthcare business (the manufacturer of Nicorette® Gum) to Johnson & Johnson.]

REMARKS/COMMENTS:

This "Supplement for Prior Approval" provides for a new flavor for Nicorette® Gums, 2mg (NDA 18-612) and 4mg (NDA 20-066). **Specifically, Nicorette® White Ice™ Mint 2mg and 4mg Coated Gum** is a line-extension to approved Nicorette® coated gum variants. The subject drug product will be manufactured by McNeil at their Helsingborg, Sweden facility. This facility

**Nicorette® Original and Mint (nicotine polacrilex) Gums, 2mg and 4mg
GlaxoSmithKline**

is already an FDA-approved site for the manufacture of currently marketed Nicorette® gum products.

Note that all of the Nicorette® coated gum products, including the subject drug product, have an

(b) (4) The main differences between currently marketed Nicorette® coated gum products and the subject drug product are the flavor and (b) (4). These modifications in the formulation are considered minor and are not expected to affect drug product stability, quality, or drug release. An *in vitro* study was performed to compare the release profile of the subject drug product with a reference formulation, Nicorette® Fruit Chill. The similarity factor obtained in the release comparison was 69. According to the criterion for this test, Nicorette® White Ice Mint is considered similar to the currently approved Nicorette Fruit Chill formulation.

With the exception of the new ingredients ((b) (4) Flavor and starch), all of the ingredients in Nicorette® (nicotine polacrilex) White Ice™ Mint 2mg and 4mg Coated Gums are identical to those used in Nicorette® (nicotine polacrilex) Cinnamon Surge™ 2mg and 4mg Coated Gums.

(b) (4) In light of this, no data were presented on the residual solvent profile of this product. For an overview of the residual solvent profile of Nicorette® (nicotine polacrilex) White Ice™ Mint 2mg and 4mg Coated Gums, refer to NDA 18-612/SCF-049 and NDA 20-066/SCF-030 for Nicorette® (nicotine polacrilex) Cinnamon Surge™ 2mg and 4mg Coated Gum, approved 02-JUL-2007.

The specifications and test methods used to release and evaluate the product on stability are equivalent to already approved specifications and test methods for currently marketed Nicorette® coated gums.

The inactive ingredients contained in Nicorette® (nicotine polacrilex) White Ice™ Mint 2mg and 4mg Coated Gum consist of polacrilex resin (b) (4) gum base, xylitol, sodium bicarbonate (2mg only), sodium carbonate, magnesium oxide, hypromellose, polysorbate 80, starch, acesulfame potassium, sucralose, menthol, peppermint oil, (b) (4) Flavor, titanium dioxide, D&C Yellow No. 10 aluminum lake (4mg only) and carnauba wax. With the exception of the flavor, all of the excipients are approved pharmaceutical grade materials (USP or USP- NF) and all have a history of in-use safety in similar products of this type. In light of this, no data are presented for any of these ingredients. The flavor ingredient, (b) (4) Flavor, contains components which are designated as substances that are generally recognized as safe (GRAS), or are approved for use by a regulation of the United States Food and Drug Administration. Exposure to these inactive ingredients from use of Nicorette® (nicotine polacrilex) White Ice™ Mint 2mg and 4mg Coated Gum is comparable to exposures from

**Nicorette® Original and Mint (nicotine polacrilex) Gums, 2mg and 4mg
GlaxoSmithKline**

similar products that are currently marketed, and therefore this product presents no significant toxicological risk.

Three pilot-scale batches of each strength of the subject drug products have been placed on stability. Satisfactory 6-month stability data, provided in the amendment's Module 3, Section 3.2.P.8, together with 24 months of data from Nicorette® Fruit Chill, support a 24-month expiry date for the proposed drug product.

CONCLUSIONS & RECOMMENDATIONS:

APPROVAL

The information submitted in the supplement and referenced DMFs adequately support the proposed changes. Approval is recommended.

(see attached electronic signature page)

J. S. Hathaway, Ph.D.
Reviewing Chemist

cc: Orig. NDA 18-612
Orig. NDA 20-066
ONP/DNP/Division File
ONDQA/DPE/Chem/JSHathaway
ONDQA/DPE/ChemPAL/LZhou
ONDQA/DPE/ChemBranchChf/HPatel
ONDQA/DPE/ProjMgr/RMcKnight

filename: C:\Documents and Settings\hathaways\My Documents\MSWordDocs\NDA
Reviews\SuppNDAs\18612\N18612r.scf.050.doc

Approval

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this page is the manifestation of the electronic signature.**

/s/

Steve Hathaway

6/4/2008 11:23:48 AM

CHEMIST

New flavoring, (b) (4) ingredients for 2mg and 4mg gums
For your concurrence

Liang Zhou

6/4/2008 11:38:31 AM

CHEMIST

For BC, Dr. H Patel Becky, It is OTC managed

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

18-612/S-050 & 20-066/S-031

OTHER REVIEW(S)



Office of Nonprescription Products
Division of Nonprescription Regulation Development

Drug Labeling Review

NDA # 18612 and 20-066	Sponsor: GlaxoSmithKline
Drug Product: Nicorette® gum 2 mg and 4 mg (White Ice Mint Gum coated)	# of Stock Keeping Units in Submission: 3 for each NDA submission
Submission Date: February 13 and 14, 2008	Review Date: June 6, 2008
Type of Submission: SCF-050 and SCF-031	Reviewer: Mary S. Robinson

Stock Keeping Unit: Nicorette (nicotine polacrilex) 4 mg White Ice Mint coated gum 20, 100, and 160 count cartons.

Background

This review is based on GlaxoSmithKline's February 13, 2008 and February 14, 2008 submission of NDA 18612/SCF-050 (2mg) and NDA 20066/SCF-031 (4 mg) gums, respectively, for Nicorette® new White Ice Mint coated gum. This submission contains full color draft printed labeling for Nicorette 2 mg and 4 mg White Ice Mint coated gum 20, 100, and 160 count cartons, annotated White Ice Mint 2 mg and 4 mg 20, 100 and 160 count cartons, White Ice Mint Carrying Case, blister card, and User's Guide. This product is a line extension to already approved Nicorette coated gum flavor variants. The sponsor states that the submitted labeling is consistent with previously approved labeling for the coated gums, with the exception of the inactive ingredients relating to the flavor and (b) (4).

On June 11, 2008 the sponsor amended (by eMail) the February 13 and 14, 2008 submissions in response to an agency inquiry about the nature of the reserved promotional text area on the cartons. The sponsor agreed to resubmit the labeling with the added promotional text. The new submission contained full color printed labeling for the 2 mg and 4 mg 20-, 100-, and 160-count cartons.

Unless otherwise noted, the reviewer's comments and recommendations refer to the labeling submitted for 2 mg and 4 mg 20-, 100-, and 160-count cartons

Reviewer's Comments

1. The 100-, and 160-count cartons include promotion text for the Quit Rewards promotional.

This is acceptable.

2. The 20 count carton includes a coupon instead of the Quit Rewards promotion.

This is acceptable.

3. The carton and "Drug Facts" labeling for the 20-, 100-, and 160-count cartons are identical to the previously approved labeling with the exception of the inactive ingredients relating to the flavor and (b) (4) in the "inactive ingredients" section. The annotated font specifications are acceptable. These labeling are acceptable. However, for consistency with the approved labeling for Nicorette coated gum flavor variants, the sponsor needs to capitalize the statement of identity phrase "STOP SMOKING AID" on the principal display panel at the time of next printing or within 180 days, whichever is sooner.

4. The carrying case label, blister card and Users' Guide Information contain no changes from the previous approved labeling. These labeling do not need to be re-approved.

Reviewer's Recommendations

1. Inform the sponsor that this supplement can be approved. Request the sponsor to submit final printed labeling, identical to the draft carton labels (20-, 100- and 160-counts) submitted on June 11, 2008, when available.

2. The carrying case label, blister card and Users' Guide Information are identical to the previous approved labeling, do not need to request to sponsor to submit final printed labeling identical to the labeling submitted on February 13 and 14, 2008.
3. Remind the sponsor to remove "NEW Flavor" on the principal display of the cartons, 6 months after introduction to the market place.
4. Request the sponsor to capitalize the statement of identity phrase "STOP SMOKING AID" on the principal display panel of for the 20-, 100-, and 160-, count cartons, at the time of next printing or within 180 days, whichever come first. This revision can be submitted in the sponsor's next annual report.

C:\data\DATA Nicotine\Nicorette White Ice Mint Gum NDA20066_S031andS050jun 6 2008DFS.doc

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this page is the manifestation of the electronic signature.**

/s/

Mary Robinson
6/12/2008 03:47:03 PM
INTERDISCIPLINARY

Marina Chang
6/12/2008 03:57:53 PM
INTERDISCIPLINARY
NDA 18-612/SCF-050: This review is superseded by the labeling
review that was DFS'ed on 6/11/08 and signed
off on 6/12/08 morning.



Office of Nonprescription Products
Division of Nonprescription Regulation Development

Drug Labeling Review

NDA # 18-612	Sponsor: GlaxoSmithKline
Drug Product: Nicorette® gum 2 mg (White Ice Mint Gum coated)	# of Stock Keeping Units in Submission: 3
Submission Date: February 13, 2008/	Review Date: June 4, 2008
Type of Submission: SCF-050	Reviewer: Mary S. Robinson

Stock Keeping Unit: Nicorette (nicotine polacrilex) 2 mg White Ice Mint coated gum 20, 100, and 160 count cartons.

Background

This review is based on GlaxoSmithKline's February 13, 2008 submission of NDA 18612/SCF-050 for Nicorette® 2 mg new White Ice Mint coated gum. This submission contains full color draft printed labeling for Nicorette 2 mg White Ice Mint coated gum 20, 100, and 160 count cartons, annotated White Ice Mint 2 mg 20, 100 and 160 count cartons, White Ice Mint Carrying Case, blister card, and User's Guide. This product is a line extension to already approved Nicorette coated gum flavor variants. The sponsor states that the submitted labeling is consistent with previously approved labeling for the coated gums, with the exception of the inactive ingredients relating to the flavor and (b) (4)

On June 11, 2008 the sponsor amended (by eMail) the February 13, 2008 submission in response to an agency inquiry about the nature of the reserved promotional text area on the cartons. The sponsor agreed to resubmit the labeling with the added promotional text. The new submission contained full color printed labeling for the 2 mg 20-, 100-, and 160-count cartons.

Unless otherwise noted, the reviewer's comments and recommendations refer to the labeling submitted for 2 mg 20-, 100-, and 160-count cartons

Reviewer's Comments

1. The 100-, and 160-count cartons include promotion text for the Quit Rewards promotional.

This is acceptable.

2. The 20 count carton includes a coupon instead of the Quit Rewards promotion.

This is acceptable.

Reviewer's Recommendations

The submitted labeling is acceptable. The sponsor maybe informed that this supplement can be approved.

However, at printing, for consistency with the approved labeling for Nicorette coated gum flavor variants, the sponsor needs to capitalize the statement of identity phrase "STOP SMOKING AID" on the principal display panel of the Nicorette 2 mg White Ice Mint coated gum 20-, 100-, and 160-, count cartons.

Also remind the sponsor to remove "NEW Flavor" after 6 months on the 2 mg 20-, 100-, and -160 count cartons

C:\data\DATA Nicotine\Nicorette\Nicorette White Ice Mint Gum NDA18612_S050 feb13 2008.doc

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

/s/

Mary Robinson
6/11/2008 03:35:11 PM
INTERDISCIPLINARY

Marina Chang
6/12/2008 08:11:50 AM
INTERDISCIPLINARY

Marina Chang
6/12/2008 08:12:56 AM
INTERDISCIPLINARY

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

18-612/S-050 & 20-066/S-031

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



GlaxoSmithKline

March 21, 2008

NDA 20-066

GlaxoSmithKline
1500 Littleton Road
Parsippany, NJ
07054-3884

Tel. 973 889 2100
Fax. 973 889 2390
www.gsk.com

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

Re: NDA 20-066/S-031
Nicorette® White Ice™ Mint 4mg Coated Gum
AMENDMENT #1: CMC – Drug Product and Drug Substance

Dear Dr. Leonard-Segal,

Reference is made to NDA 20-066, Serial No. 031 for Nicorette® White Ice Mint™ 4mg Coated Gum submitted on February 14, 2008.

The drug product manufacturer, McNeil, has amended their drug master file (DMF No. 3835) on February 25, 2008 and March 14, 2008 to tighten the nicotine related substances (NRS) specifications for the following tests based on review of 6-month stability data for Nicorette White Ice Mint 4mg Coated Gum:

(b) (4)

As a result of these updates, the proposed specifications for the subject drug product are now consistent with the currently approved Nicorette coated gum products (i.e., Freshmint, Fruit Chill and Cinnamon Surge).

Since NDA 20-066/S-031 was submitted in electronic Common Technical Document (e-CTD) format, the above-mentioned updates to the drug product are provided as replacement sections in Module 3.

In addition, an amendment to the manufacturer's drug substance drug master file (DMF No. 5757) was submitted to the Agency on February 15, 2008. The updates made to this DMF are considered minor in nature and were included in McNeil's annual report submitted on February 19, 2008. Information regarding this update to the drug substance DMF is referenced in Module 3 of this amendment.

Also enclosed are updated letters of authorization and cross reference information from McNeil. Please note that the following administrative change was made to Module 1:

- replacement of cross reference letter provided in NDA 20-066/S-031 (submitted on February 14, 2008) to reflect the correct letter provided by McNeil for the subject drug product

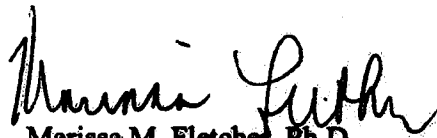
An additional administrative change was made by the Sponsor, GlaxoSmithKline (GSK) to Module 2, Section 2.7.1 (*Summary of Biopharmaceutic Studies and Associated Analytical Methods*) to correct for a typographical error.

Please note that this submission is provided in CTD format in accordance with the draft guidance titled, "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications Using the CTD Specifications," dated April 2006, and is formatted according to the folder/file structure described in the ICH M2 EWG Electronic Common Technical Document Specification v3.2 dated February 4, 2004.

This submission has been confirmed to be virus-free using Symantec AntiVirus Corporate Edition, version 10.1.0.396, scan engine 71.4.0.15, updated 3/20/2008 rev. 9, and is approximately 2.8 MB in size.

If you have any questions regarding this supplement, please call me at 973-889-4443.

Sincerely,

A handwritten signature in black ink, appearing to read "Marissa Fletcher". The signature is fluid and cursive, with the first name "Marissa" and last name "Fletcher" clearly distinguishable.

Marissa M. Fletcher, Ph.D.

Manager, Regulatory Affairs

GlaxoSmithKline Consumer Healthcare, L.P.



GlaxoSmithKline

March 21, 2008

NDA 18-612

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
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Center for Drug Evaluation and Research
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www.gsk.com

**Re: NDA 18-612/S-050
Nicorette® White Ice™ Mint 2mg Coated Gum
AMENDMENT #1: CMC – Drug Product and Drug Substance**

Dear Dr. Leonard-Segal,

Reference is made to NDA 18-612, Serial No. 050 for Nicorette® White Ice Mint™ 2mg Coated Gum submitted on February 13, 2008.

The drug product manufacturer, McNeil, has amended their drug master file (DMF No. 3835) on February 25, 2008 and March 14, 2008 to update the finished product specifications for the subject drug product as described below:

1. Tightening of the nicotine related substances (NRS) specifications for the following tests based on review of 6-month stability data:



2. Corrections to clerical errors observed in the NRS acceptance criteria for the following:

As a result of these updates, the proposed specifications for the subject drug product are now consistent with the currently approved Nicorette coated gum products (i.e., Freshmint, Fruit Chill and Cinnamon Surge).

Since NDA 18-612/S-050 was submitted in electronic Common Technical Document (e-CTD) format, the above-mentioned updates to the drug product are provided as replacement sections in Module 3.

In addition, an Amendment to the manufacturer's drug substance drug master file (DMF No. 5757) was submitted to the Agency on February 15, 2008. The updates made to this DMF are considered minor in nature and were included in McNeil's annual report submitted on February 19, 2008. Information regarding this update to the drug substance DMF is referenced in Module 3 of this Amendment.

Also enclosed are updated letters of authorization and cross reference information from McNeil. Please note that the following administrative change was made to Module 1:

- replacement of cross reference letter provided in NDA 18-612/S-050 (submitted on February 13, 2008) to reflect the correct letter provided by McNeil for the subject drug product

This submission is provided in CTD format in accordance with the draft guidance titled, "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications Using the CTD Specifications," dated April 2006, and is formatted according to the folder/file structure described in the ICH M2 EWG Electronic Common Technical Document Specification v3.2 dated February 4, 2004.

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If you have any questions regarding this supplement, please call me at 973-889-4443.

Sincerely,

A handwritten signature in black ink, appearing to read "Marissa Fletcher". The signature is fluid and cursive, with the first name "Marissa" and the last name "Fletcher" clearly distinguishable.

Marissa M. Fletcher, Ph.D.
Manager, Regulatory Affairs
GlaxoSmithKline Consumer Healthcare, L.P.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-612/S-050

PRIOR APPROVAL SUPPLEMENT

GlaxoSmithKline Consumer Healthcare
Attention: Marissa M. Fletcher, Ph.D.
Manager, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Dr. Fletcher:

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

Name of Drug Product: Nicorette (2 mg, nicotine polacrilex) gum

NDA Number: 18-612

Supplement number: 050

Date of supplement: February 13, 2008

Date of receipt: February 13, 2008

This supplemental application proposes a new White Ice Mint flavor variant and associated labeling changes.

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 April 13, 2008, in accordance with 21 CFR 314.101(a). If the application is filed, the goal date will be June 13, 2008.

Please cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any question, call Mary Lewis, Regulatory Project Manager, at (301) 796-0941.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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

/s/

Leah Christl

3/14/2008 03:04:50 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-066/S-031

PRIOR APPROVAL SUPPLEMENT

GlaxoSmithKline Consumer Healthcare
Attention: Marissa M. Fletcher, Ph.D.
Manager, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Dr. Fletcher:

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

Name of Drug Product: Nicorette (4 mg, nicotine polacrilex) gum

NDA Number: 20-066

Supplement number: 031

Date of supplement: February 14, 2008

Date of receipt: February 14, 2008

This supplemental application proposes a new White Ice Mint flavor variant and associated labeling changes.

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 April 14, 2008, in accordance with 21 CFR 314.101(a). If the application is filed, the goal date will be June 14, 2008.

Please cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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Beltsville, MD 20705-1266

If you have any question, call Mary Lewis, Regulatory Project Manager, at (301) 796-0941.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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

/s/

Leah Christl

3/14/2008 03:05:44 PM

February 14, 2008

NDA 20-066

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

Re: Nicotine Polacrilex Gum, 4mg
Supplement – Prior Approval (CMC): New flavor coated gum variant
Nicorette® White Ice™ Mint 4mg Coated Gum
NDA 20-066/S-031

Dear Dr. Leonard-Segal,

In accordance with 21 CFR 314.70(c), GlaxoSmithKline Consumer Healthcare (GSK) hereby submits a Prior Approval Supplement for Nicorette® White Ice Mint™ 4mg Coated Gum.

The subject drug product is a new flavor line extension to currently approved Nicorette coated gum variants. Please note that McNeil has deemed certain information in the Chemistry, Manufacturing, and Controls section of this Supplement to be proprietary. Therefore, cross-references to McNeil's drug master files (DMF) are provided and included in this Supplement accordingly.

This submission is provided in electronic CTD (e-CTD) format in accordance with the draft guidance titled, "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications Using the CTD Specifications," dated April 2006, and is formatted according to the folder/file structure described in the ICH M2 EWG Electronic Common Technical Document Specification v3.2 dated February 4, 2004.

This submission has been confirmed to be virus-free using Symantec AntiVirus Corporate Edition, version 10.1.0.396, scan engine 71.4.0.15, updated 2/13/08, and is approximately 12MB in size.

If you have any questions regarding this supplement, please call me at 973-889-4443.

Sincerely,

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**Marissa M. Fletcher, Ph.D.
Manager, Regulatory Affairs
GlaxoSmithKline Consumer Healthcare, L.P.**

February 13, 2008

NDA 18-612

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

**Re: Nicotine Polacrilex Gum, 2mg
Supplement – Prior Approval (CMC): New flavor coated gum variant
Nicorette® White Ice™ Mint 2mg Coated Gum
NDA 18-612/S-050**

Dear Dr. Leonard-Segal,

In accordance with 21 CFR 314.70(c), GlaxoSmithKline Consumer Healthcare (GSK) hereby submits a Prior Approval Supplement for Nicorette® White Ice Mint™ 2mg Coated Gum.

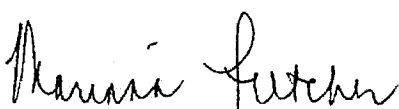
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Marissa M. Fletcher, Ph.D.
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GlaxoSmithKline Consumer Healthcare, L.P.