

GlaxoSmithKline
Research Triangle Park, NC 27709
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ZYB:XPI

MEDICATION GUIDE
ZYBAN® (zi ban)
(bupropion hydrochloride)
Sustained-Release Tablets

Read this Medication Guide carefully before you start taking ZYBAN and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment. If you have any questions about ZYBAN, ask your healthcare provider or pharmacist.

IMPORTANT: Be sure to read the three sections of this Medication Guide. The first section is about the risk of changes in thinking and behavior, depression and suicidal thoughts or actions with medicines used to quit smoking; the second section is about the risk of suicidal thoughts and actions with antidepressant medicines; and the third section is entitled “What Other Important Information Should I Know About ZYBAN?”

Quitting Smoking, Quit-Smoking Medications, Changes in Thinking and Behavior, Depression, and Suicidal Thoughts or Actions

This section of the Medication Guide is only about the risk of changes in thinking and behavior, depression and suicidal thoughts or actions with drugs used to quit smoking. Talk to your healthcare provider or your family member’s healthcare provider about:

- all risks and benefits of quit-smoking medicines.
- all treatment choices for quitting smoking.

Some people have had changes in behavior, hostility, agitation, depression, suicidal thoughts or actions while taking ZYBAN to help them quit smoking. These symptoms can develop during treatment with ZYBAN or after stopping treatment with ZYBAN.

If you, your family member, or your caregiver notice agitation, hostility, depression, or changes in thinking or behavior that are not typical for you, or you have any of the following symptoms, stop taking ZYBAN and call your healthcare provider right away:

- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- panic attacks
- feeling very agitated or restless
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- abnormal thoughts or sensations
- seeing or hearing things that are not there (hallucinations)
- feeling people are against you (paranoia)
- feeling confused
- other unusual changes in behavior or mood

When you try to quit smoking, with or without ZYBAN, you may have symptoms that may be due to nicotine withdrawal, including urge to smoke, depressed mood, trouble sleeping, irritability, frustration, anger, feeling anxious, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain. Some people have even experienced suicidal thoughts when trying to quit smoking without medication. Sometimes quitting smoking can lead to worsening of mental health problems that you already have, such as depression.

Before taking ZYBAN, tell your healthcare provider if you have ever had depression or other mental illnesses. You should also tell your healthcare provider about any symptoms you had during other times you tried to quit smoking, with or without ZYBAN.

Antidepressant Medicines, Depression and Other Serious Mental Illnesses, and Suicidal Thoughts or Actions

Although ZYBAN is not a treatment for depression, it contains bupropion, the same active ingredient as the antidepressant medications WELLBUTRIN[®], WELLBUTRIN[®] SR, and WELLBUTRIN XL[®].

This section of the Medication Guide is only about the risk of suicidal thoughts and actions with antidepressant medicines.

What is the most important information I should know about antidepressant medicines, depression and other serious mental illnesses, and suicidal thoughts or actions?

- 1. Antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, or young adults within the first few months of treatment.**
- 2. Depression or other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a particularly high risk of having suicidal thoughts or actions.** These include people who have (or have a family history of) bipolar illness (also called manic-depressive illness) or suicidal thoughts or actions.
- 3. How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?**
 - Pay close attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed.
 - Call your healthcare provider right away to report new or sudden changes in mood, behavior, thoughts, or feelings.
 - Keep all follow-up visits with your healthcare provider as scheduled. Call the healthcare provider between visits as needed, especially if you have concerns about symptoms.

Call your healthcare provider right away if you or your family member has any of the following symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling very agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

What else do I need to know about antidepressant medicines?

- **Never stop an antidepressant medicine without first talking to a healthcare provider.** Stopping an antidepressant medicine suddenly can cause other symptoms.
- **Antidepressants are medicines used to treat depression and other illnesses.** It is important to discuss all the risks of treating depression and also

the risks of not treating it. Patients and their families or other caregivers should discuss all treatment choices with the healthcare provider, not just the use of antidepressants.

- **Antidepressant medicines have other side effects.** Talk to the healthcare provider about the side effects of the medicine prescribed for you or your family member.
- **Antidepressant medicines can interact with other medicines.** Know all of the medicines that you or your family member takes. Keep a list of all medicines to show the healthcare provider. Do not start new medicines without first checking with your healthcare provider.

It is not known if ZYBAN is safe and effective in children under the age of 18.

What other important information should I know about ZYBAN?

- **Seizures: There is a chance of having a seizure (convulsion, fit) with ZYBAN, especially in people:**
 - with certain medical problems.
 - who take certain medicines.

The chance of having seizures increases with higher doses of ZYBAN. For more information, see the sections “Who should not take ZYBAN?” and “What should I tell my healthcare provider before taking ZYBAN?” Tell your healthcare provider about all of your medical conditions and all the medicines you take. **Do not take any other medicines while you are taking ZYBAN unless your healthcare provider has said it is okay to take them.**

If you have a seizure while taking ZYBAN, stop taking the tablets and call your healthcare provider right away. Do not take ZYBAN again if you have a seizure.

- **High blood pressure (hypertension). Some people get high blood pressure that can be severe, while taking ZYBAN.** The chance of high blood pressure may be higher if you also use nicotine replacement therapy (such as a nicotine patch) to help you stop smoking (see the section of this Medication Guide called “How should I take ZYBAN ?”).
- **Manic episodes.** Some people may have periods of mania while taking ZYBAN, including:
 - Greatly increased energy
 - Severe trouble sleeping
 - Racing thoughts

- Reckless behavior
- Unusually grand ideas
- Excessive happiness or irritability
- Talking more or faster than usual

If you have any of the above symptoms of mania, call your healthcare provider.

- **Unusual thoughts or behaviors.** Some patients have unusual thoughts or behaviors while taking ZYBAN, including delusions (believe you are someone else), hallucinations (seeing or hearing things that are not there), paranoia (feeling that people are against you), or feeling confused. If this happens to you, call your healthcare provider.
- **Severe allergic reactions. Some people can have severe allergic reactions to ZYBAN. Stop taking ZYBAN and call your healthcare provider right away** if you get a rash, itching, hives, fever, swollen lymph glands, painful sores in the mouth or around the eyes, swelling of the lips or tongue, chest pain, or have trouble breathing. These could be signs of a serious allergic reaction.

What is ZYBAN?

ZYBAN is a prescription medicine to help people quit smoking.

ZYBAN should be used with a patient support program. It is important to participate in the behavioral program, counseling, or other support program your healthcare professional recommends.

Quitting smoking can lower your chances of having lung disease, heart disease, or getting certain types of cancer that are related to smoking.

Who should not take ZYBAN?

Do not take ZYBAN if you:

- have or had a seizure disorder or epilepsy.
- have or had an eating disorder such as anorexia nervosa or bulimia.
- **are taking any other medicines that contain bupropion, including WELLBUTRIN, WELLBUTRIN SR, WELLBUTRIN XL, APLENZIN[®], or FORFIVO XL[™].** Bupropion is the same active ingredient that is in ZYBAN.
- drink a lot of alcohol and abruptly stop drinking, or take medicines called sedatives (these make you sleepy), benzodiazepines, or anti-seizure medicines, and you stop taking them all of a sudden.

- take a monoamine oxidase inhibitor (MAOI). Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including the antibiotic linezolid.
 - **do not take an MAOI within 2 weeks of stopping ZYBAN unless directed to do so by your healthcare provider.**
 - **do not start ZYBAN if you stopped taking an MAOI in the last 2 weeks unless directed to do so by your healthcare provider.**
- are allergic to the active ingredient in ZYBAN, bupropion, or to any of the inactive ingredients. See the end of this Medication Guide for a complete list of ingredients in ZYBAN.

What should I tell my healthcare provider before taking ZYBAN?

Tell your healthcare provider if you have ever had depression, suicidal thoughts or actions, or other mental health problems. You should also tell your healthcare provider about any symptoms you had during other times you tried to quit smoking, with or without ZYBAN. See “Quitting Smoking, Quit-Smoking Medications, Changes in Thinking and Behavior, Depression, and Suicidal Thoughts or Actions.”

- **Tell your healthcare provider about your other medical conditions, including if you:**
 - have liver problems, especially cirrhosis of the liver.
 - have kidney problems.
 - have, or have had, an eating disorder such as anorexia nervosa or bulimia.
 - have had a head injury.
 - have had a seizure (convulsion, fit).
 - have a tumor in your nervous system (brain or spine).
 - have had a heart attack, heart problems, or high blood pressure.
 - are a diabetic taking insulin or other medicines to control your blood sugar.
 - drink alcohol.
 - abuse prescription medicines or street drugs.
 - are pregnant or plan to become pregnant.
 - are breastfeeding. ZYBAN passes into your milk in small amounts
- **Tell your healthcare provider about all the medicines you take**, including prescription, over-the-counter medicines, vitamins, and herbal supplements. Many medicines increase your chances of having seizures or other serious side effects if you take them while you are taking ZYBAN.

How should I take ZYBAN?

- Start ZYBAN before you stop smoking to give ZYBAN time to build up in your body. It takes about 1 week for ZYBAN to start working.
- Pick a date to stop smoking that is during the second week you are taking ZYBAN.
- Take ZYBAN exactly as prescribed by your healthcare provider. Do not change your dose or stop taking ZYBAN without talking with your healthcare provider first.
- ZYBAN is usually taken for 7 to 12 weeks. Your healthcare provider may decide to prescribe ZYBAN for longer than 12 weeks to help you stop smoking. Follow your healthcare provider's instructions.
- **Swallow ZYBAN Tablets whole. Do not chew, cut, or crush ZYBAN Tablets.** If you do, the medicine will be released into your body too quickly. If this happens you may be more likely to get side effects including seizures. **Tell your healthcare provider if you cannot swallow tablets.**
- ZYBAN Tablets may have an odor. This is normal.
- Take your doses of ZYBAN at least 8 hours apart.
- You may take ZYBAN with or without food.
- It is not dangerous to smoke and take ZYBAN at the same time. But, you will lower your chance of breaking your smoking habit if you smoke after the date you set to stop smoking.
- You may use ZYBAN and nicotine patches (a type of nicotine replacement therapy) at the same time, following the precautions below.
 - You should only use ZYBAN and nicotine patches together under the care of your healthcare provider. Using ZYBAN and nicotine patches together may raise your blood pressure, and sometimes this can be severe.
 - Tell your healthcare provider if you plan to use nicotine patches. Your healthcare provider should check your blood pressure regularly if you use nicotine patches with ZYBAN to help you quit smoking.
- If you miss a dose, do not take an extra dose to make up for the dose you missed. Wait and take your next dose at the regular time. **This is very important.** Too much ZYBAN can increase your chance of having a seizure.
- If you take too much ZYBAN, or overdose, call your local emergency room or poison control center right away.

Do not take any other medicines while taking ZYBAN unless your healthcare provider has told you it is okay.

What should I avoid while taking ZYBAN?

- Limit or avoid using alcohol during treatment with ZYBAN. If you usually drink a lot of alcohol, talk with your healthcare provider before suddenly stopping. If

you suddenly stop drinking alcohol, you may increase your chance of having seizures.

- Do not drive a car or use heavy machinery until you know how ZYBAN affects you. ZYBAN can affect your ability to do these things safely.

What are possible side effects of ZYBAN?

ZYBAN can cause serious side effects. See the sections at the beginning of this Medication Guide for information about serious side effects of ZYBAN.

The most common side effects of ZYBAN include:

- trouble sleeping
- stuffy nose
- dry mouth
- dizziness
- feeling anxious
- nausea
- constipation
- joint aches

If you have trouble sleeping, do not take ZYBAN too close to bedtime.

Tell your healthcare provider right away about any side effects that bother you.

These are not all the possible side effects of ZYBAN. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to GlaxoSmithKline at 1-888-825-5249.

How should I store ZYBAN?

- Store ZYBAN at room temperature between 59°F and 86°F (15°C to 30°C).
- Keep ZYBAN dry and out of the light.

Keep ZYBAN and all medicines out of the reach of children.

General information about ZYBAN

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ZYBAN for a condition for which it was not prescribed.

Do not give ZYBAN to other people, even if they have the same symptoms you have. It may harm them.

If you take a urine drug screening test, ZYBAN may make the test result positive for amphetamines. If you tell the person giving you the drug screening test that you are taking ZYBAN, they can do a more specific drug screening test that should not have this problem.

This Medication Guide summarizes important information about ZYBAN. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ZYBAN that is written for health professionals.

For more information about ZYBAN, call 1-888-825-5249.

What are the ingredients in ZYBAN?

Active ingredient: bupropion hydrochloride.

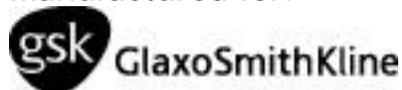
Inactive ingredients: carnauba wax, cysteine hydrochloride, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80 and titanium dioxide. The tablets are printed with edible black ink. In addition, the 150-mg tablet contains FD&C Blue No. 2 Lake and FD&C Red No. 40 Lake.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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Manufactured for:



GlaxoSmithKline

Research Triangle Park, NC 27709

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Month year

ZYB: XMG

APPENDIX A: MEDICATION GUIDE REMS

Initial REMS Approval: 02/26/2010

Most Recent Modification: 03/27/2014

NDA 20-711 ZYBAN® (bupropion hydrochloride) Sustained-Release Tablets

Smoking Cessation Aid

GlaxoSmithKline
5 Moore Drive, Durham, NC 27709
919-483-5984

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL:

The goal of this REMS is to inform patients about the potential serious risk of neuropsychiatric adverse events associated with the use of ZYBAN.

II. REMS ELEMENTS:

A. Medication Guide

GlaxoSmithKline, in accordance with 21 CFR 208.24, will make the Medication Guide available for distribution to patients. In accordance with Federal Regulations, the currently approved Medication Guide is to be dispensed with each ZYBAN prescription. Therefore, GlaxoSmithKline provides a Medication Guide attached to each unit-of-use bottle (the bottle label contains an attached extended content label containing the Medication Guide text).

Because the Medication Guide is included as part of the primary package for ZYBAN, GlaxoSmithKline has met the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

In accordance with 21 CFR 208.24(d), a statement will be included on the container label for ZYBAN to instruct pharmacists to dispense the Medication Guide with each prescription of the product.

B. Timetable for Submission of Assessments

GlaxoSmithKline will submit REMS Assessments to FDA 18 months, 3 years, and 7 years from the date of the initial approval of the REMS (February 26, 2010). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment.

GlaxoSmithKline will submit each assessment so that it will be received by the FDA on or before the due date.