

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed according to a physician's prescription only

ZYBAN

Prolonged-Release Tablets

Each tablet contains:

Bupropion hydrochloride 150 mg

For the list of inactive ingredients in the medicine, see section 6 – “Additional information”.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the physician or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

The medicine is not intended for people under 18 years of age.

1. WHAT IS THE MEDICINE INTENDED FOR?

Zyban is indicated as an aid to smoking cessation in combination with a comprehensive smoking cessation support program.

Zyban will be most effective if you are fully committed to giving up smoking. Ask a physician or pharmacist for advice on treatments and additional support that will help you stop.

Therapeutic group:

Selective noradrenaline and dopamine reuptake inhibitor.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to bupropion or any of the additional ingredients contained in this medicine (listed in section 6).

- you are taking any other medicines which contain bupropion (such as Wellbutrin XR to treat depression)
 - you have a medical problem that causes fits (seizures), such as epilepsy, or if you have a history of fits
 - you have or had in the past an eating disorder (for example, bulimia or anorexia nervosa)
 - you have severe liver problems, such as *cirrhosis*
 - you have a brain tumor
 - you are usually a heavy drinker and you have just stopped drinking alcohol, or are planning to stop while you are taking Zyban
 - you recently stopped taking sedatives or medicines to treat anxiety (especially *benzodiazepines* or similar medicines), or if you are planning to stop taking them while taking Zyban
 - you have a bipolar disorder (extreme mood swings), as Zyban could bring on an episode of this illness
 - you are taking medicines for depression or for Parkinson's disease called *monoamine oxidase inhibitors (MAOIs)*, or have taken them in the last 14 days. The timing may be shorter for some types of MAOIs – your physician will advise you on this subject.
- If any of these apply to you, talk to your physician straight away, and do not take Zyban.

Special warnings regarding use of the medicine

Talk to your physician or pharmacist before using Zyban, because some conditions make it more likely that you will have side effects (*see also section 4*).

Brugada syndrome

if you have a condition called Brugada syndrome (a rare hereditary syndrome that affects the heart rhythm) or if cardiac arrest or sudden death occurred in your family.

Children and adolescents

Zyban is not intended for people under 18 years of age.

Adults

Fits (seizures)

Zyban has been shown to cause fits (seizures) in about 1 in 1,000 people, (*see also 'Drug interactions' later in this section and section 4, 'Side effects', for more information*).

The likelihood of fits is higher if:

- **you regularly drink a lot of alcohol**
- **you have diabetes** for which you use insulin or tablets
- **you have had a serious head injury** or history of head trauma

If any of these apply to you, do not take Zyban unless you have agreed with your physician that there is a strong reason for doing so.

If you have a fit (seizure) during the treatment:

→ **Stop taking Zyban and do not take any more. Refer to your physician.**

You may have a higher risk of side effects if:

- **you have kidney or liver problems**
- **you are over the age of 65**

You will need to take a lower dosage (*see section 3*) and be checked regularly while you are taking Zyban.

If you have had mental health problems

Some people taking Zyban have had hallucinations or delusions (seeing, hearing or believing things that are not there), disordered thoughts or extreme mood swings. These effects are more likely in people who have had mental health problems before.

If you feel depressed or suicidal

Some people become depressed when they try to stop smoking; very occasionally, they may think about committing suicide, or attempt suicide. These symptoms have affected people taking Zyban, especially in the first few weeks of treatment.

If you feel depressed or think about suicide:

→ **Contact your physician or go to a hospital straight away.**

If you are taking medicines for depression

The use of these medicines together with Zyban can lead to serotonin syndrome, a potentially life-threatening condition (*see 'Drug interactions' in this section*).

High blood pressure and Zyban

Some people taking Zyban have developed high blood pressure that requires treatment. If you already have high blood pressure, it can become worse. This is more likely if you are also using **nicotine patches** to help you stop smoking.

→ **Your blood pressure will be checked** before you take Zyban and while you are taking it, especially if you already have high blood pressure. If you are also using nicotine patches, your blood pressure needs to be checked every week. If your blood pressure increases, you may need to stop taking Zyban.

Drug interactions

If you are taking, have recently taken or might take other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist.

There may be a higher than usual risk of fits if you take:

- medicines for **depression** or **other mental health problems** (see also 'Do not use the medicine if' at the beginning of section 2)
 - **theophylline** for **asthma** or **lung disease**
 - **tramadol**, a strong painkiller
 - medicines against **malaria**
 - **stimulants** or other medicines to control **your weight or appetite**
 - **steroids** (except creams and lotions for eye and skin conditions)
 - **antibiotics** called **quinolones**
 - **some types of anti-histamines** mainly used to treat allergies, that can cause sleepiness
 - medicines to treat **diabetes**.
- **If you take any medicines in this list, talk to your physician straight away** before you take Zyban (*see section 3 'Some people need to take a lower dosage'*).

Some medicines can affect how Zyban works, or increase the likelihood of getting side effects:

- medicines for **depression** (such as desipramine, imipramine, paroxetine, citalopram, escitalopram, venlafaxine) or **other mental health problems** (such as risperidone, thioridazine).

Zyban may interact with some medicines used for treatment of depression and you may experience mental status changes (e.g., agitation, hallucinations, coma), and other effects, such as body temperature above 38°C, increase in heart rate, unstable blood pressure and exaggeration of reflexes, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea).

- medicines for **Parkinson's disease** (such as levodopa, amantadine or orphenadrine)
 - **carbamazepine, phenytoin or valproate**, to treat **epilepsy** or **certain mental health problems**
 - some medicines used to treat **cancer** (such as cyclophosphamide, ifosfamide)
 - **clopidogrel**, mainly used to treat **heart disease** or **stroke**
 - some **beta blockers** (such as metoprolol), mainly used to treat high blood pressure
 - some medicines for **heart rhythm disturbances** (such as propafenone, flecainide)
 - **ritonavir** or **efavirenz**, for treatment of HIV infection.
- **If you take any medicines on this list, check with your physician.** Your physician will weigh up the benefits and risks to you of taking Zyban, or may decide to change the dosage of the other medicine you are taking.

Zyban may make other medicines less effective

- **If you take tamoxifen used to treat breast cancer**
→ **If this applies to you**, tell your physician. It may be necessary to change to another treatment for smoking cessation.
- **If you take digoxin for your heart**
→ **If this applies to you**, tell your physician. Your physician may consider adjusting the dosage of digoxin.

The dose of some medicines may need to be reduced when you stop smoking

When you smoke, the chemicals absorbed into your body can cause some medicines to be less effective. When you stop smoking, your dose of these medicines may need to be reduced; otherwise, you may experience side effects. If you are taking any other medicines, check with your physician if you notice any new symptoms that you think may be side effects.

Use of Zyban and alcohol

Some people find they are more sensitive to alcohol while taking Zyban. Your physician may suggest that you do not drink alcohol while taking Zyban, or try to drink as little as possible. If you do drink a lot now, do not just stop suddenly, because that may put you at risk of having a fit.

Effect on urine tests

Zyban may interfere with some urine tests to detect other medicines. If you need to undergo a urine test, tell your physician or hospital that you are taking Zyban.

Pregnancy and breast-feeding

Do not take Zyban if you are pregnant, think you may be pregnant or are planning to get pregnant. Ask your physician or pharmacist for advice before taking this medicine.

Some, but not all, studies have reported an increase in the risk of birth defects, particularly heart defects, in babies whose mothers were taking Zyban. It is not known if these are due to the use of Zyban.

The ingredients of Zyban can pass into breast milk. Consult your physician or pharmacist before taking Zyban.

Driving and using machines

Some of the side effects of Zyban, such as feeling dizzy or light-headed, may affect your concentration and judgement.

If you are affected, do not drive or operate machinery.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions. Check with the physician or pharmacist if you are uncertain about the preparation dosage and treatment regimen.

The dosage and treatment regimen will be determined by the physician only.

The usual dosage is:

When to start and how much to take		
<ul style="list-style-type: none">• Start taking Zyban while you are still smoking.• Set a Target Stop Smoking Day, ideally during the second week that you are taking the medicine.		
Week 1 Ideally keep smoking while taking Zyban	Days 1 to 6	Take one tablet (150 mg), once a day.
	Day 7	Increase your dose to one tablet, twice a day, at least 8 hours apart, and not near bedtime.
Week 2	Carry on taking one tablet, twice a day. Stop smoking this week, on your Target Stop Smoking Day.	
Weeks 3 to 9	Carry on taking one tablet, twice a day for up to 9 weeks. If you have not been able to stop smoking after 7 weeks, your physician will advise you to stop taking Zyban. You may be advised to stop taking Zyban gradually, after 7-9 weeks.	

Some people need to take a lower dosage as they may be more likely to develop side effects.

- if you are over the age of 65
- if you have liver or kidney disease
- if you have a higher risk of fits (*see 'Special warnings regarding the use of the medicine' and 'Drug interactions' in section 2*)

The maximum recommended dose for you is one 150 mg tablet once a day.

Do not exceed the recommended dose.

How to take your tablets

Take the Zyban tablets at least 8 hours apart. Do not take a Zyban tablet near bedtime – it may cause difficulty in sleeping.

You can take Zyban with or without food.

Swallow Zyban tablets whole. Do not chew them, crush them or split them – if you do, the medicine will be released into your body too quickly. This will make you more likely to have side effects, including fits.

If you accidentally have taken a higher dosage

If you take too many tablets, you may be more likely to have a fit or other side effects.

If you have taken an overdose or if a child has accidentally swallowed the medicine

→ **Do not delay**, refer immediately to a physician or to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine

If you forgot to take this medicine at the designated time, **do not take a double dose.** Take the next dose at the usual time and consult the physician.

Adhere to the treatment regimen recommended by your physician.

If you stop taking the medicine

You may need to take Zyban for 7 weeks to reach its full effect.

Do not stop taking Zyban without consulting the physician before stopping. You may need to reduce your dosage gradually.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the physician or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Zyban may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

Serious side effects

Fits (seizures)

Approximately 1 in every 1,000 people taking Zyban is at risk of having a fit.

Symptoms of a fit include convulsions, and usually loss of consciousness. Someone who has had a fit may be confused afterwards, and may not remember what has happened.

Fits are more likely if you take too much Zyban, if you take additional medicines, or if you are at a higher than usual risk of fits (*see section 2*).

→ **If you have a fit**, tell your physician when you have recovered. **Do not take any more Zyban.**

Allergic reactions

Rarely (at a frequency of up to 1 in 1,000 patients), people may have serious allergic reactions to Zyban. Signs of allergic reactions include:

- skin rash (including itchy, bumpy rash). Some skin rashes may need hospital treatment, especially if you also have a sore mouth or eyes
- unusual wheezing, or difficulty in breathing
- swollen eyelids, lips or tongue
- pains in muscles or joints
- collapse or blackout

→ **If you have any signs of an allergic reaction**, contact a physician at once. **Do not take any more tablets.**

Lupus skin rash or worsening of lupus symptoms

Unknown frequency – the frequency cannot be estimated from the available data in people taking Zyban.

Lupus is an immune system disorder affecting the skin and other organs.

→ **If you experience lupus flares, skin rash or lesions (particularly on sun-exposed areas) while taking Zyban**, contact your physician straight away, as it might be necessary to stop the treatment.

Acute Generalised Exanthematous Pustulosis (AGEP)

Unknown frequency – the frequency cannot be estimated from the available data in people taking Zyban.

The symptoms of AGEP include a rash with pus-filled pimples/blisters.

→ **If you have a rash that has pus-filled pimples/blisters, contact your physician straight away, as it might be necessary to stop the treatment.**

Additional side effects

Very common side effects

These may affect **more than 1 in 10** people:

- Difficulty in sleeping (make sure you do not take Zyban near bedtime)

Common side effects

These may affect **up to 1 in 10** people:

- feeling depressed (*see also 'Special warnings regarding the use of the medicine' in section 2*)
- feeling anxious or agitated
- difficulty concentrating
- a trembling sensation
- headache
- feeling nauseated, vomiting
- pain or other abdominal disturbances (such as constipation), changes in the taste of food, dry mouth
- fever, dizziness, sweating, skin rash (sometimes due to an allergic reaction), itching

Uncommon side effects

These may affect **up to 1 in 100** people:

- ringing in the ears, visual disturbances
- increase in blood pressure (sometimes severe), flushing
- loss of appetite (*anorexia*)
- feeling weak
- chest pain
- feeling confused

- rapid heartbeat

Rare side effects

These may affect **up to 1 in 1,000** people:

- fits (*see the beginning of this section*)
- twitching, muscle stiffness, uncontrolled movements, problems with walking or coordination (*ataxia*)
- palpitations
- fainting, feeling faint when you stand up suddenly, because your blood pressure falls
- feeling irritable or hostile; strange dreams (including nightmares)
- loss of memory
- tingling or numbness
- severe allergic reactions; rash together with joint and muscle pain (*see the beginning of this section*)
- urinating more, or less, than usual
- severe skin rashes that may occur in the mouth and other parts of the body and can be life-threatening
- worsening of psoriasis (thickened patches of red skin)
- yellowing of your skin or the whites of your eyes (jaundice), increase in liver enzymes, hepatitis
- changes in blood sugar levels
- A sense of detachment from reality or strangeness (*depersonalization*); seeing or hearing things that are not there (hallucinations)

Very rare side effects

These may affect **up to 1 in 10,000** people:

- restlessness, aggressiveness
- sensing or believing things that are not true (delusions); severe suspiciousness (*paranoia*)
- urinary incontinence (involuntary urination, leakage of urine)

Side effects of unknown frequency

Other side effects have occurred in a small number of people but their exact frequency is unknown:

- thoughts of self-harm or suicidal thoughts while taking Zyban or soon after stopping treatment (*see section 2, 'Before using the medicine'*). If you have these thoughts, **contact your physician or go to a hospital straight away.**
- loss of contact with reality and inability to think or judge clearly (*psychosis*); other symptoms may include hallucinations and/or delusions.
- stuttering.
- reduced numbers of red blood cells (anaemia), reduced numbers of white blood cells (leucopenia) and reduced numbers of platelets (thrombocytopenia).
- reduced blood sodium levels (hyponatremia)
- Change in mental status (e.g., agitation, hallucinations, coma), and other effects, such as body temperature above 38°C, increase in heart rate, unstable blood pressure and exaggeration of reflexes, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea), while taking Zyban together with medicines used for treatment of depression (such as paroxetine, citalopram, escitalopram, fluoxetine and venlafaxine).

Effects of smoking cessation

People who stop smoking are often affected by nicotine withdrawal. This can also affect people taking Zyban. Signs of nicotine withdrawal include:

- difficulty in sleeping
- tremor or sweating
- feeling anxious, agitated or depressed, sometimes with thoughts of suicide.

Talk to your physician if you have any concerns about how you feel.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult with the physician.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage

(www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il/>

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Do not store above 25°C.
- Store in the original package.
- Do not discard medicines in the wastewater or household waste bin. Ask the pharmacist how to dispose of medicines that are no longer in use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

- In addition to the active ingredient bupropion hydrochloride, the medicine also contains:

Tablet core:

Microcrystalline cellulose, hypromellose, cysteine hydrochloride monohydrate, magnesium stearate.

Tablet coating:

Hypromellose, titanium dioxide (E171), macrogol 400, carnauba wax.

Printing ink:

Iron oxide black (E172), hypromellose (E464).

- What the medicine looks like and the content of the package:
Zyban 150 mg tablets are white, film-coated, biconvex, round tablets imprinted with "GX CH7" on one side, in carton packages containing 10, 30, 60 or 100 tablets.
Not all pack sizes may be marketed.
- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: Glaxo Wellcome S.A., Burgos, Spain.

- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 118-33-29919.

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