BUPROPION (Systemic)

Introduction

Interim revision:

INN: Amfebutamone 4

VA CLASSIFICATION (Primary/Secondary)¾CN609/AD600

Commonly used brand name(s):Wellbutrin; Wellbutrin SR; Zyban.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

Category

Antidepressant; smoking cessation adjunct.

Indications

Accepted

Depressive disorder, major (treatment)¾Bupropion is indicated for the treatment of major depression 2, 14.

Treatment of acute depressive episodes typically requires 6 to 12 months of antidepressant therapy 10.

Patients with recurrent or chronic depression may require long-term treatment 10.

Nicotine dependence (treatment adjunct)¾The extended-release formulation of bupropion is indicated as an aid to smoking cessation treatment 6.

A smoking cessation program should include behavioral interventions, counseling, and/or other support services 6.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Chemical group¾Aminoketone 2.

Bupropion is structurally related to phenylethylamines and closely resembles diethylpropion 2.

Molecular weight¾Bupropion hydrochloride: 276.21 4

Solubility¾Highly soluble in water 2, 6.

Mechanism of action/Effect:

Antidepressant¾ Although the exact mechanism of antidepressant action is unclear, it is thought to be mediated by bupropion"s noradrenergic and/or dopaminergic effects 2, 26.

Bupropion is a weak inhibitor of neuronal uptake of norepinephrine, serotonin, and dopamine 2, 6, 26 , although inhibition of uptake occurs at doses higher than those required for bupropion"s antidepressant effects 5, 18, 26.

Hydroxybupropion, an active metabolite of bupropion, has weak norepinephrine reuptake blocking activity but it reaches concentrations high enough to produce significant norepinephrine blockade and may have clinically significant antidepressant effects 26.

Animal studies have suggested that bupropion"s antidepressant activity may be mediated through noradrenergic pathways involving the locus ceruleus 18.

Bupropion and hydroxybupropion reduce the firing rates of noradrenergic neurons in the locus ceruleus in a dose-dependent manner; this action is similar to that of the tricyclic antidepressants 26.

Bupropion shows little affinity for the serotonergic transport system 26 , and it does not inhibit monoamine oxidase 2, 6, 26.

Smoking cessation adjunct¾ Although the exact mechanism of smoking cessation action is unclear, it is thought to be mediated by bupropion"s noradrenergic and/or dopaminergic effects 6.

Bupropion increases extracellular dopamine concentrations in the nucleus accumbens 26 , as do all known addictive substances including nicotine 27.

The nucleus accumbens, a part of the mesolimbic dopamine system, may be an important component of the neural circuitry of reward 26, 27.

Also, as nicotine concentrations drop with abstinence, the firing rates of noradrenergic neurons in the locus ceruleus increase 7 , which may be the basis of withdrawal symptoms 7, 27.

Bupropion and its active metabolite, hydroxybupropion, reduce the firing rates of noradrenergic neurons in the locus ceruleus in a dose-dependent manner 26.

Other actions/effects:

Although animal studies indicate that bupropion may be an inducer of hepatic microsomal enzymes, a study in humans using a dosage of 150 mg three times a day for 14 days found no evidence of autoinduction 32.

May produce dose-related central nervous system (CNS) stimulation 14.

Absorption:

Approximately 80%; rapidly absorbed from the gastrointestinal tract 5 ; however, extensive presystemic metabolism 3 limits bioavailability 6.

Food increases extent of absorption insignificantly 6.

Distribution:

Readily crosses the blood-brain barrier and placenta 5 ; a study of one subject demonstrated that bupropion and its metabolites are distributed into breast milk 33.

Protein binding:

Bupropion¾High (84%) 6, 32 , to human plasma proteins 32.

Hydroxybupropion¾High (77%) 32.

Biotransformation:

Bupropion is extensively metabolized 6 , including presystemic metabolism 3.

Three metabolites have shown activity in animal studies 6.

Hydroxybupropion, formed principally by the cytochrome P450 2B6 (CYP2B6) isoenzyme, is comparable in potency to bupropion 6.

Threohydrobupropion and erythrohydrobupropion, amino-alcohol isomers formed by hydroxylation and/or reduction, are one tenth to one half as potent as bupropion 6.

Half-life:

Distribution¾ 3 to 4 hours 2, 6.

Elimination¾ Bupropion: Single-dose 32 mean, approximately 14 (range, 8 to 24) hours 3, 15.

Single-dose studies demonstrate a first-order elimination pattern with a mean total body clearance of approximately 2 liters per hour per kilogram of body weight 3, 15.

Bupropion: Steady-state mean, 21 ± 9 hours 32.

Hydroxybupropion: Mean, approximately 20 hours 6.

Onset of action:

Antidepressant¾1 to 3 weeks 5 ; full effect may require 4 or more weeks to achieve 2.

Time to peak concentration:

Prompt-release formulation¾ Bupropion: Approximately 1.5 hours 32, 14 , followed by biphasic decline 5, 14.

Hydroxybupropion: Approximately 3 hours 32.

Extended-release formulation¾ Bupropion: Approximately 3 hours 6.

Hydroxybupropion: Approximately 6 hours 6.

Time to steady-state concentration

Bupropion¾Within 5 days 6.

Hydroxybupropion¾Within 8 days 6.

Steady-state plasma concentration

Mean maximum concentration of bupropion was 136 nanograms per mL (0.492 micromoles per L) in healthy volunteers following a 150-mg dose of the extended-release tablet every 12 hours 6.

Peak plasma concentration of hydroxybupropion at steady-state is approximately 10 times that of bupropion 6.

Elimination:

Renal¾ Less than 1% excreted in urine unchanged 3, 5.

Over 60% excreted as metabolites within 24 hours, over 80% within 96 hours 5.

Fecal¾ Less than 10% excreted in feces 5, 15 , primarily as metabolites 6.

Precautions to Consider

Carcinogenicity

In a lifetime study of rats, there was an increase in nodular proliferative lesions of the liver at doses of 100 mg to 300 mg per kg of body weight (mg/kg; approximately 3 to 10 times the maximum recommended human dose [MRHD] on a mg per square meter of body surface area [mg/m 2] basis) a day. However, whether such lesions may be precursors of neoplasms of the liver has not been resolved. Similar lesions were not seen in studies with mice given doses of up to 150 mg/kg a day (approximately two times the MRHD on a mg/m 2 basis). 6, 14

Tumorigenicity

Studies in rodents showed no increase in malignant tumors of the liver or other organs 14.

Mutagenicity

In two of five strains in the Ames bacterial mutagenicity test, bupropion produced a mutation rate of two to three times the control mutation rate. In one of three in vivo bone marrow cytogenetic studies in rats, bupropion produced chromosomal aberrations. 6

Pregnancy/Reproduction

Fertility¾Studies in rats and rabbits given doses of up to 300 mg/kg a day have shown no evidence of impaired fertility 14.

Pregnancy¾Adequate and well-controlled studies in humans have not been done 14.

However, bupropion readily crosses the placenta 5.

Studies in rats and rabbits given doses of up to 15 to 45 times the human daily dose have not shown that bupropion causes adverse effects in the fetus. In rabbits, two studies showed a slightly increased incidence of fetal abnormalities; however, there was no increase in any specific abnormality. 14

FDA Pregnancy Category B 6, 14.
Labor and delivery¾The effect of bupropion on labor and delivery in humans is unknown 14.

Breast-feeding

Bupropion accumulates in breast milk 33 , and the potential exists for serious adverse reactions (such as seizures 19, 20, 21) in the infant 6, 14.

The milk-to-plasma ratio of bupropion in one nursing mother who was receiving 100 mg of the prompt-release formulation of bupropion three times a day ranged from 2.51 to 8.58 over 6 hours, with the peak breast-milk concentration occurring 2 hours after bupropion dosing. The bupropion metabolite threohydrobupropion also accumulated in breast milk, with a milk-to-plasma ratio ranging from 1.23 to 1.57 over the same 6 hours. Hydroxybupropion concentrations in milk did not exceed corresponding plasma concentrations at any of the measure times. Neither bupropion nor its metabolites were detectable in serum taken from the infant, a 14-month-old boy, 3.75 hours after nursing, which occurred 9.5 hours after the mother"s last dose of bupropion. No adverse effects were observed in the infant. 33

Pediatrics

Studies that included a small number of patients 6 to 16 years of age have not demonstrated pediatrics-specific problems that would limit the usefulness of bupropion in children 6.

However, there is not sufficient evidence to establish safety and efficacy of bupropion in children up to 18 years of age 2, 6.

Geriatrics

In general, studies that included patients 60 years of age and older have not demonstrated geriatrics-specific problems that would limit the usefulness of bupropion in the elderly. However,

one pharmacokinetic study has suggested that the elderly may be at increased risk for accumulation of bupropion and its metabolites. 6 Older patients are known to be more sensitive to the anticholinergic, sedative, and cardiovascular side effects of antidepressants 2, 14.

In addition, elderly patients are more likely to have age-related renal or hepatic function impairment, which may require dosage adjustment in patients receiving bupropion.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: The cytochrome P450 2B6 (CYP2B6) isoenzyme is involved in the metabolism of bupropion to its active metabolite hydroxybupropion 2, 6.

A potential exists for interactions between bupropion and medications that affect CYP2B6, such as orphenadrine and cyclophosphamide 2, 6.

Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

>> Alcohol

(concurrent use of or the cessation of chronic use of 22 alcohol during therapy may lower the seizure threshold and increase the risk of seizures; patients should be advised to minimize alcohol consumption or avoid the use of alcohol completely 2, 6, 14)

Enzyme inducers, hepatic, cytochrome P450 (see Appendix II)

(concurrent use with bupropion may increase the metabolism of bupropion 6, 13, 14 ; a study in patients receiving chronic carbamazepine therapy showed significant decreases in bupropion peak plasma concentration and area under the plasma concentration-time curve [AUC] and increases in hydroxybupropion peak plasma concentration and AUC 32 ; a study in cigarette smokers showed no effect of smoking on the pharmacokinetics of bupropion 6)

Enzyme inhibitors, hepatic, cytochrome P450 (see Appendix II)

(these medications may inhibit hepatic microsomal enzymes, thereby decreasing metabolism and increasing serum concentrations of bupropion 6, 13, 14 , thus increasing the risk of seizures 19 ; a study in patients receiving chronic valproic acid therapy showed no change in bupropion concentrations but increases in hydroxybupropion peak concentration and AUC 32)

Levodopa

(concurrent use with bupropion may result in a greater incidence of adverse effects 8 ; small initial doses of bupropion and gradual dosage increases are recommended during concurrent therapy 6, 14)

>> Monoamine oxidase (MAO) inhibitors, including furazolidone, procarbazine, and selegiline

(concurrent use of bupropion with these medications may increase the risk of acute toxicity of bupropion and is contraindicated 2, 6 ; a medication-free interval of at least 14 days should elapse between discontinuation of the MAO inhibitor and initiation of bupropion therapy 2, 6)

Nicotine

(although a nicotine transdermal system may be used concurrently with bupropion in the treatment of nicotine dependence, the combination has been associated with hypertension 6 ; blood pressure should be monitored in patients receiving this combination 6)

>> Ritonavir

(although there is no experience with the combination, ritonavir has a high affinity for several cytochrome P450 isoenzymes 1, 25 and may increase bupropion plasma concentrations, thus increasing the risk of seizures 25 ; concurrent use should be approached with caution until more information is available 12, 29)

>> Seizure-threshold-lowering medications, other, such as:

Antidepressants, tricyclic 24 or

Clozapine 16, 24 or

Corticosteroids, glucocorticoid and/or mineralocorticoid 2, 6, 14 or

Fluoxetine 15 or

Haloperidol 24 or

Lithium 24 or

Loxapine 24 or

Maprotiline 15, 24 or

Molindone 24 or

Phenothiazines 24 or

Theophylline 2, 6, 14 , or

Thioxanthenes 24 or

Trazodone 15

(concurrent use of these medications with bupropion may increase the risk of major motor seizures 3, 14, 15 ; in addition, changes in treatment regimen, such as abrupt discontinuation of a benzodiazepine, may precipitate a seizure 6, 17)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

With physiology/laboratory test values

White blood cell count

(decreased by 10 to 14% during the first 2 months of therapy 3 in one study 18 ; unknown clinical significance 3)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist

>> Anorexia nervosa, or history of or

>> Bulimia, or history of

(increased risk of seizures in patients with current or prior diagnosis of these conditions 2, 6)

>> Seizure disorders

(increased risk of seizures 2)

Risk-benefit should be considered when the following medical problems exist

Bipolar disorder

(mania may be precipitated during the depressed phase in patients with manic-depressive illness 2, 14)

>> CNS tumor or

>> Head trauma or

>> Neurologic impairment, including developmental delay 10 , or

>> Spontaneous seizures, history of

(increased risk of seizures 2, 6)

Drug abuse

(patients with a history of amphetamine or stimulant abuse may be attracted to bupropion because of its mild amphetamine-like activity, especially at higher doses 6 ; however, risk of seizures has prevented adequate testing 2, 5)

(risk of seizures may be increased in patients with addiction to opiates, cocaine, or stimulants 6)

>> Heart disease

(higher plasma concentrations of the active metabolites of bupropion may occur in patients with left ventricular dysfunction 2 ; in a short-term study of 36 patients with left ventricular impairment, ventricular arrhythmias, and/or conduction disease, mean systolic supine blood pressure readings increased by 5 ± 10 mm Hg, mean diastolic supine blood pressure readings increased by 3 ± 5 mm Hg, and two patients with mild hypertension at baseline discontinued use due to exacerbation of hypertension 23)

>> Hepatic function impairment or

>> Renal function impairment

(metabolism or excretion may be altered 2, 6, 14 ; bupropion treatment should be initiated at a reduced dosage 2 and patient should be monitored closely 2)

Hypertension 29

(may be exacerbated 23)

Psychosis, especially schizoaffective disorder, depressed 5

(latent psychosis 14 or mania 16 may be activated in susceptible patients 2)

Sensitivity to bupropion 2, 6

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):

Blood pressure

(recommended in patients who are using a nicotine transdermal system concurrently with bupropion 6 and in patients with baseline hypertension 29)

Careful supervision of depressed patients with suicidal tendencies

(recommended especially during early weeks of treatment for depression; hospitalization may be required as a protective measure 14)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Those indicating need for medical attention

Incidence more frequent

Agitation 2, 6; anxiety 2, 6

Incidence less frequent

Headache, severe 2; skin rash 2, 6 , hives 2 , or itching 6; tinnitus 2 buzzing or ringing in ears)

Incidence rare

Fainting 6; neuropsychiatric effects, including confusion 2; delusions 2 false beliefs that are not changed by facts); hallucinations 2, 14 seeing, hearing, or feeling things that are not there); paranoia 2 extreme distrust); or trouble in concentrating 2, 6; seizures 6¾especially with higher doses

Note: The risk of seizures with bupropion may be greater than with other antidepressants. Seizures occur more frequently at higher doses. The incidence with use of the extended-release formulation is approximately 0.1% (3/3100 patients) at doses of up to 300 mg a day, and 0.4% (4/1000 patients) at a dose of 400 mg a day 2.

With the use of the prompt-release formulation, seizure frequencies of 0.4% (13/3200 patients) at doses of 300 to 450 mg a day and almost tenfold higher at doses between 450 mg and 600 mg a day have been reported. 2, 17

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Abdominal pain 2; anorexia 2, 6 (decrease in appetite); constipation 6, 14; dizziness 2, 6; dryness of mouth 2, 6; increased sweating 2, 6; insomnia 2, 6 (trouble in sleeping); myalgia 2 (muscle pain); nausea or vomiting 2, 6; pharyngitis 2 (sore throat); tremor 2, 6 (trembling or shaking); weight loss, unusual 2

Note: Dryness of mouth and insomnia may be dose-related 6.

Avoiding taking bupropion at bedtime may help to relieve insomnia 6.

Incidence less frequent or rare

Blurred vision 6; drowsiness 6; palpitation 2, 6 (feeling of fast or irregular heartbeat); taste perversion 6 (change in sense of taste); unusual feeling of well-being 2; urinary frequency 2, 6

Overdose

For specific information on the agents used in the management of bupropion overdose, see:
- Benzodiazepines (Systemic) monograph; and/or
- Charcoal, Activated (Oral-Local) monograph.

For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing).

Clinical effects of overdose

Note: Deaths have occurred following massive overdose with bupropion alone 2, 6.

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Acute

Hallucinations 2, 6 seeing, hearing, or feeling things that are not there); loss of consciousness 2, 6, 9; nausea 6, 30; seizures 2, 6, 9, 30; tachycardia 6, 9, 30 fast heartbeat)¾possibly progressing to bradycardia or asystole 9, 30; vomiting 6, 9, 30

Note: Seizures occur in about one third of bupropion overdose cases 30.

Treatment of overdose

To decrease absorption¾In comatose or stuporous patients, initiation of airway intubation followed by gastric lavage within the first 12 hours of ingestion, when absorption is not yet complete 2, 6, 30.

Administration of activated charcoal every 6 hours within the first 12 hours of ingestion 2, 6, 30.

Ipecac syrup should not be used to induce vomiting because of the possibility of seizures 29, 30.

Specific treatment¾Treatment of seizures with an intravenous benzodiazepine 2, 6 , although seizures may be resistant to benzodiazepine treatment 9.

Monitoring¾Monitoring ECG and EEG for at least 48 hours 2, 6, 30.

Monitoring acid-base 9 and electrolyte balance 9 in patients presenting in status epilepticus.

Supportive care¾Maintenance of patent airway 9 and adequate ventilation 30.

Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

Note: Diuresis, dialysis, and hemoperfusion are not likely to be of benefit 2, 30 due to the slow diffusion of bupropion and its metabolites from tissue to plasma 32.

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Bupropion (Systemic) .

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Sensitivity to bupropion

Pregnancy¾Crosses placenta

Breast-feeding¾Accumulates in breast milk; because of potential for serious adverse effects in the infant, use is not recommendedContraindicated medications¾MAO inhibitors

Other medications, especially alcohol, other seizure-threshold-lowering medications, or ritonavir

Other medical problems, especially anorexia nervosa, bulimia, CNS tumor, head trauma, heart disease, hepatic or renal function impairment, history of spontaneous seizures, neurologic impairment, or seizure disorders

Proper use of this medication

>> Compliance with therapy; not taking more or less medication than prescribed

>> Taking doses of prompt-release tablets at least 4 hours apart; taking doses of extended-release tablets at least 8 hours apart to avoid occurrence of seizures

>> Swallowing extended-release tablets whole; not crushing, breaking, or chewing

Taking with food if needed to lessen gastrointestinal irritation

For smoking cessation

Taking bupropion for 7 or more days prior to the date on which smoking will be discontinued 6

Participating in smoking cessation support program, including behavioral interventions, counseling, and/or other support 6

For mental depression

May require 4 weeks or longer for optimal antidepressant effects 2

Continuing to take bupropion after feeling better, as directed by physician, to help prevent recurrence

>> Proper dosing

Missed dose: For extended-release and prompt-release tablets¾Skipping the missed dose and returning to regular dosing schedule 28, 32 ; not doubling doses 31

>> Proper storage

Precautions while using this medication

Regular visits to physician to check progress during therapy

>> Not taking bupropion within 14 days of taking an MAO inhibitor

>> Not taking bupropion under different brand names concurrently, because of dose-dependent incidence of seizures

>> Minimizing or avoiding consumption of alcoholic beverages to reduce the risk of seizures 14

>> Possible dizziness, drowsiness, or euphoria; caution when driving, using machinery, or doing other things requiring alertness and judgment 2, 14

Side/adverse effects

Signs of potential side effects, especially agitation; anxiety; severe headache; skin rash, hives, or itching; tinnitus; fainting; neuropsychiatric effects; or seizures

General Dosing Information

Bupropion is marketed under different brand names for different approved indications 2, 6 ; patients should not receive bupropion under different brand names concurrently due to the dose-dependent incidence of seizures 6.

To reduce the risk of agitation, anxiety, and insomnia, which are more frequent at initiation of therapy, increases in dosage must be made gradually 2.

Seizures occur more frequently at higher doses; the incidence with use of the extended-release formulation is approximately 0.1% (3/3100 patients) at doses of up to 300 mg a day, and 0.4% (4/1000 patients) at a dose of 400 mg a day 2.

With use of the prompt-release formulation, seizure frequencies of 0.4% (13/3200 patients) at doses of 300 to 450 mg a day and almost tenfold higher at doses between 450 mg and 600 mg a day have been reported. 2, 17

Patients being treated for nicotine dependence should continue to smoke during the first week of treatment with bupropion to allow the medication to reach steady-state plasma concentrations 6.

A target date for discontinuation of smoking should be set for the second week of treatment 6.

Bupropion treatment should be continued for 7 to 12 weeks 6.

Longer treatment may be considered in individual patients 6.

If significant progress toward abstinence is not seen by the seventh week of therapy, the current attempt to quit smoking is unlikely to be successful and discontinuation of bupropion should be considered 6.

Full antidepressant action may not be evident for 4 weeks or longer 2.

Potentially suicidal patients should not have access to large quantities of this medication 2 since depressed patients, particularly those who use alcohol excessively, may continue to exhibit suicidal tendencies until significant improvement occurs 2.

Diet/Nutrition

Bupropion may be taken with food to lessen gastrointestinal irritation 18.

Bioequivalence information

At steady-state, the prompt-release and the extended-release formulations of bupropion hydrochloride are bioequivalent with respect to both rate and extent of absorption 2.

For prevention of seizures

The risk of seizures may be reduced if:

· The total daily dose of the prompt-release formulation does not exceed 450 mg 14 and the total daily dose of the extended-release formulation does not exceed 400 mg when used as an antidepressant 2 and 300 mg when used as an aid to smoking cessation 6.

· Each single dose of the prompt-release formulation 14 or the extended-release formulation, when used as an aid to smoking cessation 6 , does not exceed 150 mg 6, 14 , and each single dose of the extended-release formulation does not exceed 200 mg when used as an antidepressant 2.

· Doses of the prompt-release formulation are taken at least 4 hours apart 14 and doses of the extended-release formulation are taken at least 8 hours apart 2, 6.

· The dosage is increased gradually 2, 14.

· Caution is used in patients with a history of seizures, cranial trauma, or other predisposition to seizures 2, 6 , and during concurrent use with other medications or treatment regimens, such as the abrupt discontinuation of benzodiazepines, that may lower the seizure threshold 2, 6.

For treatment of adverse effects

Recommended treatment consists of the following:
· For agitation, anxiety, or insomnia¾Lowering dosage, and then increasing it gradually as needed and tolerated 2, 5.

Temporary sedative-hypnotic medication may be necessary 2 , but is usually not required beyond the first week of treatment 2.

Avoiding a bedtime bupropion dose may minimize insomnia 2.

If effects are severe, discontinuation of bupropion may be necessary 14.

· For nausea and vomiting¾Taking with meals, or decreasing and then gradually increasing the dosage 5.

Oral Dosage Forms

BUPROPION HYDROCHLORIDE EXTENDED-RELEASE TABLETS

Usual adult dose

Antidepressant¾Oral, initially 150 mg once a day in the morning for three days, then 150 mg two times a day if well tolerated 2.

If no improvement is seen after several weeks, dosage may be increased to 200 mg two times a day 2.

Note: Doses should be taken at least eight hours apart to reduce the risk of seizures 2.

Smoking cessation adjunct¾Oral, initially 150 mg once a day for three days, then 150 mg two times a day for seven to twelve weeks 6.

Note: Doses should be taken at least eight hours apart to reduce the risk of seizures 6.

Usual adult prescribing limits

Antidepressant¾400 mg per day, with no single dose exceeding 200 mg 2.

Smoking cessation adjunct¾300 mg per day, with no single dose exceeding 150 mg 6.

Usual pediatric dose

Safety and efficacy have not been established in children younger than 18 years of age [2, 6].

Strength(s) usually available

U.S.¾100 mg (Rx)[Wellbutrin SR (carnauba wax) (cysteine hydrochloride) (FD&C Blue No. 1 Lake) (hydroxypropyl methylcellulose) (magnesium stearate) (microcrystalline cellulose) (polyethylene glycol) (polysorbate 80) (titanium dioxide) 2]

150 mg (Rx)[Wellbutrin SR (carnauba wax) (cysteine hydrochloride) (FD&C Blue No. 2 Lake) (FD&C Red No. 40 Lake) (hydroxypropyl methylcellulose) (magnesium stearate) (microcrystalline cellulose) (polyethylene glycol) (polysorbate 80) (titanium dioxide) 2] [Zyban (carnauba wax) (cysteine hydrochloride) (FD&C Blue No. 2 Lake) (FD&C Red No. 40 Lake) (hydroxypropyl methylcellulose) (magnesium stearate) (microcrystalline cellulose) (polyethylene glycol) (polysorbate 80) (titanium dioxide) 6]

Canada¾100 mg (Rx)[Wellbutrin SR (carnauba wax) (cysteine hydrochloride) (FD&C Blue No. 1 Lake) (hydroxypropyl methylcellulose) (magnesium stearate) (microcrystalline cellulose) (polyethylene glycol) (polysorbate 80) (titanium dioxide) 34]

150 mg (Rx)[Wellbutrin SR (carnauba wax) (cysteine hydrochloride) (FD&C Blue No. 2 Lake) (FD&C Red No. 40 Lake) (hydroxypropyl methylcellulose) (magnesium stearate) (microcrystalline cellulose) (polyethylene glycol) (polysorbate 80) (titanium dioxide) 34] [Zyban (carnauba wax) (cysteine hydrochloride) (FD&C Blue No. 2 Lake) (FD&C Red No. 40 Lake) (hydroxypropyl methylcellulose) (magnesium stearate) (microcrystalline cellulose) (polyethylene glycol) (polysorbate 80) (titanium dioxide) 35]

Packaging and storage:

Store at controlled room temperature, 20 to 25 °C (68 to 77 °F) [2, 6], in a tight, light-resistant container [2, 6], unless otherwise specified by manufacturer.

Auxiliary labeling:

- Avoid alcoholic beverages.
- Swallow tablet whole. Do not break or chew.

Additional information:

Bupropion is marketed under different brand names for different approved indications [2, 6]; patients should not receive bupropion under different brand names concurrently due to the dose-dependent incidence of seizures [6].

Note: Bupropion hydrochloride may have a characteristic odor [6].

BUPROPION HYDROCHLORIDE TABLETS

Usual adult dose

Antidepressant¾Oral, initially 100 mg two times a day, the dosage being increased gradually, no sooner than three days after beginning therapy, to 100 mg three times a day as needed and tolerated 14.

Note: Doses should be taken at least four hours apart to reduce the risk of seizures 14.

Usual adult prescribing limits

450 mg per day, with no single dose exceeding 150 mg 14.

Usual pediatric dose

Safety and efficacy have not been established in children younger than 18 years of age 14.

Strength(s) usually available

U.S.¾75 mg (Rx)[Wellbutrin (D&C Yellow No. 10 Lake) (FD&C Yellow No. 6 Lake) (hydroxypropyl cellulose) (hydroxypropyl methylcellulose) (light mineral oil) (microcrystalline cellulose) (talc) (titanium dioxide) 14]

100 mg (Rx)[Wellbutrin (FD&C Red No. 40 Lake) (FD&C Yellow No. 6 Lake) (hydroxypropyl cellulose) (hydroxypropyl methylcellulose) (light mineral oil) (microcrystalline cellulose) (talc) (titanium dioxide) 14]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Auxiliary labeling:

· Avoid alcoholic beverages.

Additional information:

Bupropion is marketed under different brand names for different approved indications 2, 6 ; patients should not receive bupropion under different brand names concurrently due to the dose-dependent incidence of seizures 6.

Note: Bupropion hydrochloride may have a characteristic odor 6.