Prescribing Information

PrPARNATE®

tranylcypromine sulfate
Tablets

ANTIDEPRESSANT

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4

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Prescribing Information

PrPARNATE®

(tranylcypromine sulfate) Tablets

10 mg

Antidepressant

Clinical Pharmacology

Tranylcypromine is a non-hydrazine monoamine oxidase (MAO) inhibitor with a rapid onset of activity. It increases the concentration of epinephrine, norepinephrine, and serotonin in storage sites in the nervous system. In theory, the increased concentration of monoamines in the brainstem is the basis for its antidepressant activity.

Tranylcypromine differs from other MAO inhibitors in being a reversible inhibitor. When tranylcypromine is withdrawn, monoamine oxidase activity is generally restored within a week, although the drug is excreted in 24 hours.

Indications and Clinical Use

PARNATE® has been used successfully to treat psychotic depressive states such as: depressive phase of manic-depressive psychosis, involutional melancholia, reactive depression and psychoneurotic depression of moderate to severe intensity.

In the psychiatric treatment of severe endogenous depression, it is impossible to predict, with presently known data, which patients will respond best to PARNATE® and which to electroconvulsive therapy (ECT). The drug may be indicated in some reactive depressions in which ECT is not indicated.

PARNATE® is not recommended for use in mild depressive states resulting from temporary situational difficulties.

Note: Because PARNATE® is a potent agent with the capability of producing serious side effects (e.g., hypertensive crises, sometimes complicated by fatal intracranial bleeding); its use should be reserved for patients who can be closely supervised.

Before prescribing PARNATE®, the physician should be thoroughly familiar with information on its dosage, side effects, and contraindications, as well as the principles of MAO inhibitor therapy and the side effects of this class of drugs as reported in the literature. The physician should also be familiar with the symptomatology of mental depression and alternate methods of treatment to aid in the careful selection of patients for PARNATE® therapy.

Selecting the Patient:

1. PARNATE® should be used for the symptomatic treatment of moderate to severe depression. It is not recommended for those mild depressive reactions where more conservative therapy is indicated.

2. PARNATE® should be reserved for those patients who can be followed closely. Blood pressure should be recorded periodically to detect evidence of pressor response to PARNATE® therapy.

3. PARNATE® should not be used in patients with cerebrovascular or cardiovascular disorders (e.g., arteriosclerosis, hypertension). (See CONTRAINDICATIONS.)

4. PARNATE® should not be used in patients receiving any other antidepressant medication. (See CONTRAINDICATIONS.)

5. PARNATE® is not recommended for patients with a history of recurring or frequent headaches, especially the tension and vascular types.

6. PARNATE® should not be used alone in patients with marked psychomotoragitation, since it is recognized that antidepressant drugs can aggravate some co-existing symptoms such as agitation or anxiety.

PARNATE® combined with trifluoperazine: PARNATE® has been combined with trifluoperazine, in the treatment of co-existing anxiety and depression. Such combined therapy has been found particularly valuable when used to treat depressed patients in whom a persistent disorder of mood is associated with anxiety, moderate agitation, inappropriate mental symptoms (such as unnatural fears or suspicions and phobias) or improper response to single-agent therapy.

Combined PARNATE®- trifluoperazine therapy has been used successfully in the treatment of psychiatric conditions such as psychoneurotic depression, agitated depression, schizo-affective disorders and pseudoneurotic schizophrenia. If the patient appears to have a pure depression, PARNATE® should be used alone and, similarly, if the symptoms appear to indicate a pure anxiety state, trifluoperazine should be used first. The combined therapy has frequently displayed striking effectiveness in patients who obtained little benefit from treatment with a succession of single drugs.

For comprehensive prescribing information on trifluoperazine, refer to Prescribing Information on that product.

Contraindications

PARNATE® is Contraindicated:

In patients with a previous history of hypersensitivity to tranylcypromine or excipients.

In patients with cerebrovascular or cardiovascular disorders or a history of recurrent or frequent headaches. PARNATE® should not be administered to patients with confirmed or suspected cerebrovascular defect, hypertension or cardiovascular disease. The drug should be used with caution in individuals beyond the age of 60 because of the possibility of existing cerebral sclerosis with damaged vessels.

In patients with liver damage or blood dyscrasias. Extensive clinical use and laboratory tests have revealed no evidence of liver toxicity or blood dyscrasias due to PARNATE® therapy. Because rare cases of hepatitis have been reported, it is recommended that patients with known liver damage or blood dyscrasias should not be treated with PARNATE®.

In pheochromocytoma. PARNATE® should not be used in the presence of known or suspected pheochromocytoma, as such tumours secrete pressor substances.

In combination with certain drugs. Because the effect of many antidepressant drugs may persist for 10 to 20 days, do not commence PARNATE® therapy within less than a week of discontinuing treatment with such drugs; then use half the normal dosage for the first week. Similarly, allow one week to elapse between the discontinuance of PARNATE® and the administration of any other drug that is contraindicated with PARNATE® such as:

1. Other monoamine oxidase inhibitors (MAOIs) such as isocarboxazid and phenelzine sulfate.

2. Dibenzazepine derivatives such as amitriptyline, nortriptyline, protriptyline, desipramine, imipramine, doxepin, perphenazine, carbamazepine, cyclobenzaprine, amoxapine, maprotiline and trimipramine, as combination with these drugs may induce hypertensive crises or severe convulsive seizures.

3. Sympathomimetics including amphetamines, ephedrine, methyldopa, dopamine, and levodopa; as well as tryptophan. These may result in potentiation, precipitating hypertension, severe headache, and hyperpyrexia. Cerebral (subarachnoid) hemorrhage may also occur. These compounds may be found in many herbal preparations, as well as over-the-counter drugs, such as cold, hay fever, energy-enhancing and weight-reducing preparations. The combination of MAOIs and tryptophan has been reported to cause behaviour and neurologic syndromes including disorientation, confusion, amnesia, delirium, agitation, hypomanic signs, ataxia, myoclonus, hyperreflexia, shivering, ocular oscillations and Babinski signs.

4. SSRIs or SNRIs (eg. venlafaxine): There have been reports of serious, sometimes fatal reactions when MAOIs are given before, with, or shortly after discontinuation with some SSRIs or SNRIs. It is recommended that MAOIs are not used in combination with SSRIs or SNRIs. If SSRIs or SNRIs are used consecutively, a suitable washout period should be observed. The following is a guide, but prescribing information for individual products should be consulted:

- MAOI followed by SSRI or SNRI (eg. venlafaxine) - 2 weeks
- Fluoxetine followed by MAOI - 5 weeks
- Other SSRI followed by MAOI - 2 weeks
- SNRI (eg. venlafaxine) followed by MAOI – 1 week

5. Other drugs: dextromethorphan, buspirone HCl.

In combination with foods with a high tyramine content.

Tyramine is normally metabolized by monoamine oxidase in the intestinal and hepatic cells. When monoamine oxidase is inhibited, tyramine absorbed from the gastrointestinal tract passes freely into the circulation. It releases norepinephrine from adrenergic neurones causing exaggerated hypertensive and other effects.

When excessive amounts of tyramine are consumed in conjunction with PARNATE®, or within 2 weeks of stopping treatment, a serious and sometimes fatal hypertensive reaction may occur.

Tyramine occurs naturally in some foods or may occur from the bacterial breakdown of protein in foods which are fermented, aged or spoiled.

Foods that have reliably been shown to contain a high tyramine content and may also have been reported to induce a serious hypertensive reaction when consumed with PARNATE® are contraindicated.

Foods that are contraindicated in combination with PARNATE®:

- All matured or aged cheeses (exceptions: fresh cottage cheese, cream cheese, ricotta and processed cheese). All non-cheese dairy products can be consumed providing they are fresh.
- All aged, cured or fermented meat, fish or poultry (note: meat, fish or poultry that has not undergone aging, curing or fermenting and that is bought fresh, stored correctly and eaten fresh is not contraindicated).
- All fermented soybean products (e.g. soy sauce, miso, fermented tofu).

- Sauerkraut.
- Fava or broad bean pods.
- Banana peel (but not the pulp).
- Concentrated yeast extracts (e.g. Marmite spread).
- All tap/draught beers (Note: some bottled beers, including non-alcoholic beer, may also pose a risk).

Patients should be advised to minimize or avoid use of all alcoholic beverages while taking PARNATE®.

Patients should be advised to adhere to the following dietary guidance about eating fresh foods:

Foods may be deliberately aged as part of their processing and these are contraindicated (see list above). Foods may also naturally age over time, even if they are refrigerated. It is therefore extremely important that patients are instructed to buy and eat only fresh foods or those which have been properly frozen. They should avoid eating foods if they are unsure of their storage conditions or freshness and they should be cautious of foods of unknown age or composition even if refrigerated.

The longer food is left to deteriorate and the larger the quantity of food eaten, the greater the potential quantity of tyramine ingested. Where there is any doubt, patients should be advised to either avoid the food or consume in strict moderation if it is not otherwise contraindicated.

Patients should also be warned that tyramine levels may vary by brand or even batch and a person may absorb different amounts of tyramine from a particular food at different times. Therefore, if they have accidentally consumed a prohibited food on one occasion and not had a reaction, this does not mean that they will not have a serious hypertensive reaction if they consume the same food on a different occasion.

Warnings

Hypertensive crisis: The most important adverse reaction associated with PARNATE® is hypertensive crisis, which has sometimes been fatal. This response is not usually dose-related. It is associated with a distinctive reaction characterized by some or all of the following symptoms: occipital headache which may radiate frontally, palpitation, neck stiffness or soreness, nausea or vomiting, sweating (sometimes with fever and sometimes with cold, clammy skin) with early pallor followed later by flushing, and photophobia. Either tachycardia or bradycardia may be present, sometimes associated with constricting chest pain. Mydriasis may occur.

The occipital headache, together with pain and stiffness in the cervical muscles, may mimic subarachnoid hemorrhage, but can equally be associated with actual intracranial bleeding, as in other conditions where a sudden rise in blood pressure occurs. Cases of such bleeding have been reported, some of which have been fatal.

Blood pressure should be followed closely in patients taking PARNATE® to detect evidence of any pressor response. It is emphasized that full reliance should not be placed on blood pressure readings, but that the patient should also be observed frequently.

Therapy should be discontinued immediately upon the occurrence of palpitation or frequent headache during PARNATE® therapy. These signs may be prodromal of a hypertensive reaction. Patients should be instructed to report promptly the occurrence of headache or other symptoms.

If a hypertensive reaction occurs, PARNATE® should be discontinued and therapy to lower blood pressure should be given immediate consideration. Headache tends to abate as blood pressure decreases. On the basis of present evidence, phentolamine is recommended for use in acute cases. (the dosage reported for phentolamine is 5 mg I.V. administered slowly.) Do not use parenteral reserpine or rauwolfia alkaloids for the treatment of a hypertensive crisis as they may, by releasing catecholamines, exacerbate the condition. Care should be taken to administer these drugs in such a way as to avoid producing an excessive hypotensive effect. Fever should be managed by means of

external cooling. Other symptomatic and supportive measures may be desirable in particular cases. Acute distress generally subsides in 24 hours or less. For milder reactions, the more moderate adrenolytic action of injectable chlorpromazine may be more appropriate.

Hypotension, which may be postural, has been observed during PARNATE® therapy, particularly at doses above 30 mg daily. It is seen most commonly (but not exclusively) in patients with pre-existing hypertension. In most instances, it affects the systolic readings. Rare instances of syncope have been seen. Dosage increases should be made more gradually in patients showing a tendency toward hypotension at the starting dose. Postural hypotension can usually be relieved by having the patient lie down until blood pressure returns to normal. This side effect is usually temporary, but if it persists, PARNATE® should be discontinued. Blood pressure usually returns rapidly to pre-treatment levels upon discontinuation of PARNATE®.
Also, when PARNATE® is combined with those phenothiazine derivatives or other compounds known to cause hypotension, the possibility of additive hypotensive effects should be considered.

Potential Association with the Occurrence of Behavioral and Emotional Changes, Including Self-Harm:

It is unknown whether increased risk of suicidal ideation and behavior is associated with the use of PARNATE® in pediatric patients and/ or adults.

However, recent analyses of placebo-controlled clinical trial safety databases from SSRIs and other newer antidepressants suggest that use of these drugs in patients under the age of 18 may be associated with behavioral and emotional changes, including an increased risk of suicidal ideation and behavior over that of placebo. Thus, rigorous clinical monitoring for suicidal ideation or other indicators of potential for suicidal behavior is advised in patients of all ages given any antidepressant drug. This includes monitoring for emotional and behavioral changes.

Clinical worsening and suicide risk in adults with psychiatric disorders: Patients with depression may experience worsening of their depressive symptoms and/or the emergence of suicidal ideation and behaviours (suicidality) whether or not they are

taking antidepressant medications. This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored for clinical worsening (including development of new symptoms) and suicidality, especially at the beginning of a course of treatment, or at the time of dose changes, either increases or decreases. It is general clinical experience with all antidepressant therapies that the risk of suicide may increase in the early stages of recovery.

Patients with a history of suicidal behaviour or thoughts, and those patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are at a greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

Patients (and caregivers of patients) should be alerted about the need to monitor for any worsening of their condition (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour or thoughts of harming themselves and to seek medical advice immediately if these symptoms present. It should be recognised that the onset of some neuropsychiatric symptoms could be related either to the underlying disease state or the drug therapy (see Mania and bipolar disorder below).

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients who experience clinical worsening (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Mania and bipolar disorder: A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone can increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

As with all antidepressants, tranylcypromine should be used with caution in patients with a history of mania.

Precautions

Interactions with Other Drugs (see also CONTRAINDICATIONS): In general, the physician should bear in mind the possibility of a lowered margin of safety when PARNATE® is administered in combination with potent drugs and should adjust dosage carefully.

A marked potentiating effect has been reported on some central nervous system depressants such as morphine, meperidine, barbiturates and alcohol. For this reason, narcotics and barbiturates should be used conservatively with PARNATE®, and patients should be warned that the drug may poteniate the effects of alcoholic beverages.

Caution should be exercised when giving PARNATE® with hypotensive agents: guanethidine, as its action may be antagonized; reserpine, as hyperactivity may occur; alpha-methyldopa, since the combination may give rise to central excitation.

When PARNATE® is combined with those phenothiazine derivatives or other compounds known to affect blood pressure, patients should be observed more closely because of the possibility of additive hypotensive effects.

Caution should also be exercised when giving PARNATE® with antiparkinson agents, as the combination may result in potentiation, with profuse sweating, tremulousness, and a rise in body temperature.

Drugs which lower the seizure threshold, including MAO inhibitors, should not be used with metrizamide. As with other MAOIs, PARNATE® should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours after the procedure.

Caution should be exercised when giving PARNATE® with clomipramine hydrochloride, as this drug, in combination with a MAOI, has been reported to result in hyperpyrexia, diffuse intravascular coagulation, and status epilepticus; and pethidine, as this drug in combination with a MAOI may lead to an increase of serotonin associated effects which could cause serotonin toxicity.

PARNATE® should be administered with caution to patients receiving disulfiram. In a single study, rats given high intraperitoneal doses of d- or l-isomers of tranylcypromine sulfate plus disulfiram experienced severe toxicity including convulsions and death. Additional studies in rats given high oral doses of racemic tranylcypromine sulfate and disulfiram produced no adverse interaction.

PARNATE® may affect ability to drive or operate machinery.

In Angina: MAOIs may have the capacity to suppress anginal pain that would otherwise serve as a warning of myocardial ischemia.

In Depression: PARNATE® may aggravate coexisting symptoms in depression, such as anxiety and agitation. In depressed patients, the possibility of suicide should always be considered and adequate precautions taken. Exclusive reliance on drug therapy to prevent suicidal attempts is unwarranted, as there may be a delay in the onset of therapeutic effect or an increase in anxiety and agitation. Also, some patients fail to respond to drug therapy or may respond only temporarily.

In Diabetes: Some MAOIs have contributed to hypoglycemic episodes in diabetic patients receiving insulin or oral hypoglycemic agents. Therefore, PARNATE® should be used with caution in diabetics under treatment with these drugs.

In Epilepsy: Because the influence of PARNATE® on the convulsive threshold is variable in animal experiments, suitable precautions should be taken if epileptic patients are treated.

In Hyperthyroidism: Use PARNATE® with caution in hyperthyroid patients because of their increased sensitivity to pressor amines.

In Renal Dysfunction: The usual precautions should be observed in patients with impaired renal function, since there is a possibility of cumulative effects in such patients.

In Pregnancy and Lactation: PARNATE® has been shown to pass through the placental barrier to the fetus of the rat and into the milk of the lactating dog. Nevertheless, as with any potent drug, the physician must assess the definite medical need when prescribing

for the pregnant patient. Adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available.

In Surgery: It is suggested that PARNATE® be discontinued at least seven days before elective surgery to allow time for recovery of monoamine oxidase activity before anesthetic agents are given.

Drug Dependency: There have been reports of drug dependency in patients using doses of PARNATE® significantly in excess of the therapeutic range. Some of these patients had a history of previous substance abuse.

Adverse Reactions

The most frequently seen side effect is insomnia, which can usually be overcome by giving the last dose of the day not later than 3 p.m., by reducing the dose, or by prescribing a mild hypnotic.

Some of the following unwanted reactions have been reported in the literature; others are possible. They are classified according to their seriousness and probable cause - an arrangement intended to help the physician view them in proper perspective.

Pharmacologic Reactions of a Serious Nature:

A. Hypertensive crisis: (See WARNINGS.)

B. Hypotension: (See WARNINGS.)

C. Overstimulation which may include increased anxiety, agitation, and manic symptoms, is usually evidence of excessive therapeutic action. Dosage should be reduced, or a phenothiazine tranquilizer should be administered concomitantly.

Pharmacologic Reactions of a Less Serious Nature: Patients may experience restlessness, insomnia, drowsiness, dizziness, weakness, dry mouth, nausea, abdominal pain, anorexia, diarrhea or constipation. Tachycardia, palpitation, blurred vision, headache without blood pressure elevation; chills, sweating, urinary retention, edema and impotence have each been reported in at least one patient.

Hematologic or Allergic Reactions: Blood dyscrasias, including anemia, leukopenia, agranulocytosis, and thrombocytopenia have been reported. Rare instances of hepatitis (e.g., one case of mild jaundice, not of the serious type associated with hydrazine MAOIs) and skin rash have been reported.

Other Reactions: Micturation difficulty has been reported. Tinnitus, muscle spasm and tremors, paresthesia and habituation have been reported so rarely that the role of PARNATE® cannot be established. Alopecia has been reported very rarely.

Drug Dependency: There have been reports of drug dependency in patients using PARNATE® tablets (see **PRECAUTIONS**). Symptoms reported after stopping PARNATE® include: sleep disturbances, depression, confusion, delirium, tremor, agitation, convulsion, anxiety, hallucinations, fatigue, headache.

For management of a suspected drug overdose contact your regional Poison Control Centre.

Symptoms and Treatment of Overdosage

Symptoms:

The characteristic symptoms that may arise as a result of PARNATE® overdosage are usually those which have already been described under **WARNINGS** and **ADVERSE REACTIONS**. However, an intensification of these symptoms and sometimes severe additional manifestations may be seen, depending on the degree of overdosage and on individual susceptibility.

Some patients exhibit insomnia, restlessness and anxiety, progressing in severe cases to agitation, mental confusion and incoherence. Hypotension, dizziness, weakness and drowsiness may occur, progressing in severe cases to extreme dizziness and shock. A few patients have displayed hypertension with severe headache and other symptoms. Rare instances have been reported in which hypertension was accompanied by twitching or myoclonic fibrillation of skeletal muscles with hyperpyrexia, sometimes progressing to generalized rigidity and coma.

Treatment:

Treatment normally consists of general supportive measures, close observation of vital signs and steps to counteract specific symptoms as they occur. The management of hypertensive reactions is described under **WARNINGS**. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

External cooling is recommended if hyperpyrexia occurs. Barbiturates have been reported to help myoclonic reactions, but frequency of administration should be controlled carefully because PARNATE® may prolong barbiturate activity.

When hypotension requires treatment, the standard measures for managing circulatory shock should be initiated. If pressor agents are required, noradrenaline is the most suitable. The rate of infusion should be regulated by careful observation of the patient. MAOIs may sometimes increase the pressor response as has been demonstrated with levarterenol. Mephentermine may be required if marked refractory hypotension occurs.

Although PARNATE® is rapidly excreted; its MAO inhibiting action may persist for approximately one week.

Dosage and Administration

Dosage should be adjusted to the requirements of the individual patient. If the patient responds to therapy, the response is usually seen within 48 hours to three weeks after starting medication.

- Recommended starting dosage is 20 mg per day – 10 mg in the morning and 10 mg in the afternoon.
- Continue this dosage for 2 to 3 weeks.
- If no signs of a response appear, increase dosage to 30 mg daily – 20 mg upon arising and 10 mg in the afternoon.

- Continue this dosage for at least one week. If no improvement occurs, continued administration is unlikely to be beneficial. Although dosages above 30 mg per day have been used, it should be borne in mind that the incidence and severity of side effects may increase as dosage is raised. Dosage increases should be made in increments of 10 mg per day and ordinarily at intervals of one to three weeks.

- When a satisfactory response is obtained, dosage may be reduced to a maintenance level.

- Some patients will be maintained on 20 mg per day; many will need only 10 mg daily.

- Reduction from peak to maintenance dosage may be desirable before withdrawal. If withdrawn prematurely, original symptoms will recur. No tendency to produce rebound depressions of greater intensity has been seen, although this is a theoretical possibility in patients treated at high doses. Experimental work indicates that PARNATE® is rapidly excreted. Inhibition of MAO activity may, however, persist for up to one week.

- Combined PARNATE® - trifluoperazine therapy: For those physicians wishing to combine PARNATE® with trifluoperazine, the usual dosage is PARNATE® 10 mg plus trifluoperazine 1 mg or 2 mg twice daily (morning and afternoon) depending on the individual patient requirements. After a satisfactory response is secured, medication can often be reduced to one dose daily, usually administered in the morning. Patients displaying marked mental disturbance - especially psychotic - manifestations or severe agitation - will usually require larger initial doses of trifluoperazine.

- Children and adolescents (less than 18 years of age): PARNATE® is not indicated for use in children or adolescents aged less than 18 years (see Warnings and Precautions).

Note: When ECT is being administered concurrently with PARNATE®, 10 mg BID can usually be given during the series, then reduced to 10 mg daily for maintenance therapy.

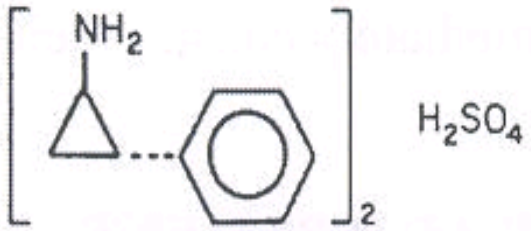
Pharmaceutical Information

Drug Substance

Proper Name: tranylcypromine sulfate

Chemical Name: (±)-*trans*-2-phenylcyclopropylamine sulfate (2:1)

Structural Formula:



and enantiomer

Molecular Formula: $(C_9H_{11}N)_2.H_2SO_4$

Molecular Weight: 133.19 (free base)

364.47 (sulfate salt)

Description: A white or almost white, crystalline powder; odourless or with a faint odour similar to that of cinnamaldehyde.

Soluble in water, very slightly soluble in ethanol (96%) and in ether, insoluble in chloroform.

Composition

Each PARNATE® 10 mg tablet contains 10 mg of tranylcypromine and the non-medicinal ingredients: carnuaba wax, citric acid, croscarmellose sodium, D&C red No. 7, edible black printing ink, FD&C Blue No. 2, FD&C yellow No. 6, gelatin, hydroxy propylmethyl cellulose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol 400, purified water, talc and titanium dioxide.

Stability and Storage Recommendations

PARNATE® tablet should be stored at 15-30°C.

Availability of Dosage Forms

PARNATE® (tranylcypromine sulfate) 10mg tablets:

Each biconvex, rose-red, round film-coated tablet, with PARNATE® and SB monogram printed in black on one side, is available in bottles of 100 tablets.

PART III: CONSUMER INFORMATION

PrPARNATE®
Tranylcypromine Sulfate

This leaflet is part III of a three-part "Product Monograph" published for PARNATE®, approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PARNATE®. Contact your doctor or pharmacist if you have any questions about the drug.

Please read this information before you start to take your medication, even if you have taken this drug before. Keep this information with your medicine in case you need to read it again.

ABOUT THIS MEDICATION

What the medication is used for:
PARNATE® has been prescribed to you by your doctor to relieve your symptoms of depression.

What it does:
PARNATE® belongs to the family of medicines called monoamine oxidase inhibitors (MAOIs). PARNATE® increases the levels of naturally occurring chemicals in the brain called epinephrine, norepinephrine, and serotonin, thus relieving the symptoms of depression.

When it should not be used:
PARNATE® should not be used:

- if you are allergic to the active ingredient, tranylcypromine or any of the components of its formulation (See What the medicinal ingredient is and What the nonmedicinal ingredients are section)
- if you have high blood pressure or heart disease
- if you have ever had a stroke, or any other kind of cerebrovascular disorder
- if you have liver disease or blood dyscrasias (i.e. blood disorders)
- if you have a history of severe or frequent headaches.
- if you have a pheochromocytoma (a tumor of the adrenal gland)
- if you are receiving any other antidepressant medication

What the medicinal ingredient is:
The medical ingredient in PARNATE® is tranylcypromine sulfate.

What the nonmedicinal ingredients are:
PARNATE® contains the following nonmedicinal ingredients: carnauba wax, citric acid, croscarmellose sodium, gelatine, hydroxyl propylmethyl cellulose, lactose, magnesium stearate, propylene glycol, talc and titanium dioxide.

What dosage forms it comes in:
PARNATE® is available as a round, film-coated tablet. Each tablet contains 10 mg tranylcypromine sulfate.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- **New or Worsened Emotional or Behavioral Problems: Particularly in the first few weeks or when doses are adjusted, a small number of patients taking drugs of this type may feel worse instead of better; for example, they may experience unusual feelings of agitation, hostility or anxiety, or have impulsive or disturbing thoughts such as thoughts of self-harm or harm to others. Should this happen to you, or to those in your care if you are a caregiver or guardian, consult your doctor immediately. Close observation by a doctor is necessary in this situation. Do not discontinue your medication on your own.**

- **Hypertensive crisis: Certain foods and drinks must be avoided during treatment with PARNATE® and for two weeks after stopping treatment. This hypertensive reaction can be life-threatening, depending on the amount of tyramine that has been taken (See INTERACTIONS WITH THIS MEDICATION).**

BEFORE you use PARNATE®, tell your doctor or pharmacist:

- all your medical conditions, including a history of stroke, liver disease, blood disorders, kidney disease, heart problems, diabetes, epilepsy, or overactive thyroid gland
- if you have or have ever had recurrent or frequent headaches
- any medications (prescription or non prescription) which you are taking or have recently taken, especially any other antidepressants
- if you are pregnant, plan to become pregnant, or are breastfeeding
- if you are beyond the age of sixty
- your habits of alcohol and /or street drug consumption
- if you had any type of surgery or are planning to have surgery

Effects on Pregnancy and Newborns:
As stated above, ask your doctor or pharmacist for advice before taking any medicine including PARNATE®. If you are already taking/using PARNATE® and have just found out that you are pregnant, you should talk to your doctor immediately. You should also talk to your doctor if you are planning to become pregnant.

Children and adolescents (less than 18 years of age):
Treatment with antidepressants is associated with an increased risk of suicidal thinking and behaviour in children and adolescents with depression.

INTERACTIONS WITH THIS MEDICATION

Check with your doctor or pharmacist before taking any other medicines, including prescription and non-prescription medicines. Some medicines may cause serious unwanted effects if you take them at the same time as PARNATE®. This also applies even in the first weeks after you stop taking PARNATE®.

Drugs that may interact with PARNATE® include:
- other antidepressants, such as other MAOIs, selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitor (SNRI) and certain tricyclic antidepressants
- appetite suppressants such as amphetamines
- cold or any hay fever medicines (including nose drops or sprays)
- cough suppressant such as dextromethorphan
- levodopa and other treatments for Parkinson's disease
- herbal preparations
- other drugs that affect serotonin such as pethidine and tryptophan
- medications which lower blood pressure, including guanethidine, reserpine, methyldopa
- narcotics and barbiturates

Certain foods and drinks must be avoided during treatment with PARNATE® and for two weeks after stopping treatment. PARNATE® reacts with a chemical, tyramine, found in various foods, which can cause dangerously high blood pressure (See Serious Warnings and Precautions). This reaction can be life-threatening, depending on the amount of tyramine that has been taken. You should avoid foods in which aging or breakdown is used to increase flavour, including:
- matured or aged cheeses
- aged, cured or fermented meat, fish or poultry
- fermented soybean products, such as soy sauce
- sauerkraut
- fava or broad bean pods
- banana peel (but not the pulp)
- concentrated yeast extracts
- all tap/draught beers
- in general, drinking alcoholic beverages should be kept to a minimum or avoided completely while taking PARNATE®.

Pre-prepared foods such as pizzas, casseroles, meals with sauces, and some restaurant foods may contain these prohibited foods or drink. It is therefore important that you check the ingredients of foods or drink that you have not prepared yourself.

All foods that you eat must be fresh, or properly frozen. Tyramine levels of many foods also increase naturally as they get older, even if they are refrigerated. It is very important that you buy and eat only fresh foods or those which have been properly frozen.

The amounts of tyramine may vary in different brands or even batches of food. A person may absorb different amounts of tyramine from a particular food at different times. Therefore, if you have accidentally taken a prohibited food or drink on one occasion and not had a reaction, you can still have a serious reaction if you take it again.

Your doctor has more information on foods to be careful with or avoid while taking PARNATE®. Ask your doctor for advice if you have any questions about this.

PROPER USE OF THIS MEDICATION

Usual dose:
- It is important that you take PARNATE® exactly as your doctor has instructed. The usual starting dose of PARNATE® is one 10 mg tablet taken twice a day.
- PARNATE® tablets are usually taken in the morning and again mid-afternoon. It is better if you take your tablets at the same times each day.
- You should continue to take your medicine even if you do not feel better, as it may take a number of weeks for your medicine to work.
- Keep taking your tablets, as instructed, until the doctor tells you to stop.
- Talk to your doctor before you stop taking your medication on your own.

Remember: This medicine has been prescribed only for you. Do not give it to anybody else, as they may experience undesirable effects, which may be serious.

Overdose:
If you have taken a large number of tablets all at once, go to the nearest hospital emergency department immediately, even though you may not feel sick. Show the doctor your pack of tablets.

Missed Dose:
If you forget to take a PARNATE® tablet, do not try to make up for the dose that you missed by taking more than one dose at a time. Wait until the next dose and take your normal dose then.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medications, PARNATE® can cause some side effects. You may not experience any of them. For most patients these side effects are likely to be minor and temporary. However, some may be serious. Consult your doctor if you experience these or other side effects, as the dose may have to be adjusted.

If you experience an allergic reaction (including skin rash, hives, swelling, trouble breathing) or any severe or unusual side effects, stop taking the drug and go to the nearest hospital emergency department immediately.

The most common side effects of PARNATE® are:
- sleep disturbances (insomnia)
- nausea
- dry mouth
- drowsiness
- weakness
- dizziness
- loss of appetite
- diarrhea
- constipation

PARNATE® does not usually affect people's normal activities. However, some people feel drowsiness, dizziness or light headedness while taking it, in which case they should not drive or operate machinery.

Tell your doctor immediately if you notice any of the following:
- severe dizziness or fainting on standing
- fast heartbeat
- unusual bleeding or bruising
- agitation, confusion or nervousness
- muscle spasms or twitches
- difficulty passing urine

Stop taking PARNATE® and contact your doctor or go to the emergency department of your nearest hospital if the following happens:
- severe or frequent headaches, chest pain, fast or slow heartbeat, neck stiffness or soreness, sweating with initial paleness followed by flushing of the skin, enlarged pupils, nausea and vomiting.

Other rare side effects that have been reported include disorders of the liver and blood.

New or Worsened Emotional or Behavioral Problems
Particularly in the first few weeks or when doses are adjusted, a small number of patients taking drugs of this type may feel worse instead of better; for example, they may experience unusual feelings of agitation, hostility or anxiety, or have impulsive or disturbing thoughts such as thoughts of self-harm or harm to others. Should this happen to you, or to those in your care if you are a caregiver or guardian, consult your doctor immediately. Close observation by a doctor is necessary in this situation. Do not discontinue your medication on your own. See also the WARNINGS and PRECAUTIONS sections.

Drug Dependence and Discontinuation Symptoms
It is possible to become dependent on PARNATE®. You may experience unwanted effects when you stop taking PARNATE®. Withdrawal symptoms such as sleep disturbances, depression, confusion, agitation, hallucinations and other symptoms have been reported after stopping treatment of PARNATE®. Tell your doctor as soon as possible if you have these or any other symptoms. Contact your doctor before stopping or reducing your dosage of PARNATE®.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect		**Talk with your doctor or pharmacist**	**Seek immediate medical emergency assistance.**
Rare	Allergic reactions including but not limited to red and lumpy skin rash, hives, swelling in the mouth, tongue, face and throat, itching, rash, trouble breathing		✓
See Warnings & Precautions	New or Worsened Emotional or Behavioral Problems	✓	
	Hypertensive crisis [severe or frequent headaches, chest pain, fast or slow heartbeat, neck stiffness or soreness, sweating with initial paleness followed by flushing of the skin, enlarged pupils, nausea and vomiting]		✓

This is not a complete list of side effects. For any unexpected effects while taking PARNATE®, contact your doctor or pharmacist.

HOW TO STORE IT

PARNATE® should be stored between 15 and 30°C. Keep PARNATE® out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701E
    Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

http://www.gsk.ca or by contacting the sponsor,

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