PT:L68

PRESCRIBING INFORMATION

PARNATE®

brand of

tranylcypromine sulfate

tablets 10 mg

Suicidality in Children and Adolescents

Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of *Parnate* or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. *Parnate* is not approved for use in pediatric patients. (See WARNINGS and PRECAUTIONS—Pediatric Use.)

Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with major depressive disorder (MDD), obsessive compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4,400 patients) have revealed a greater risk of adverse events representing suicidal thinking or behavior (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. No suicides occurred in these trials.

DESCRIPTION

Chemically, tranylcypromine sulfate is (±)-*trans*-2-phenylcyclopropylamine sulfate (2:1).

Each round, rose-red, film-coated tablet is imprinted with the product name PARNATE and SB and contains tranylcypromine sulfate equivalent to 10 mg of tranylcypromine. Inactive ingredients consist of cellulose, citric acid, croscarmellose sodium, D&C Red No. 7, FD&C Blue No. 2, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, iron oxide, lactose, magnesium stearate, talc, titanium dioxide and trace amounts of other inactive ingredients.

ACTION

Tranylcypromine is a non-hydrazine monoamine oxidase inhibitor with a rapid onset of activity. It increases the concentration of epinephrine, norepinephrine and serotonin in storage sites throughout the nervous system and, in theory, this increased concentration of monoamines in the brain stem is the basis for its antidepressant activity. When tranylcypromine is withdrawn, monoamine oxidase activity is recovered in 3 to 5 days, although the drug is excreted in 24 hours.

INDICATIONS

For the treatment of Major Depressive Episode Without Melancholia.

Parnate (tranylcypromine sulfate) should be used in adult patients who can be closely supervised. It should rarely be the first antidepressant drug given. Rather, the drug is suited for patients who have failed to respond to the drugs more commonly administered for depression.

The effectiveness of *Parnate* has been established in adult outpatients, most of whom had a depressive illness which would correspond to a diagnosis of Major Depressive Episode Without Melancholia. As described in the American Psychiatric Association's Diagnostic and Statistical Manual, third edition (DSM III), Major Depressive Episode implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning and includes at least 4 of the following 8 symptoms: change in appetite, change in sleep, psychomotor agitation or retardation, loss of interest in usual activities or decrease in sexual drive, increased fatigability, feelings of guilt or worthlessness, slowed thinking or impaired concentration and suicidal ideation or attempts.

The effectiveness of *Parnate* in patients who meet the criteria for Major Depressive Episode with Melancholia (endogenous features) has not been established.

SUMMARY OF CONTRAINDICATIONS

Parnate (tranylcypromine sulfate) should not be administered in combination with any of the following: MAO inhibitors or dibenzazepine derivatives; sympathomimetics (including amphetamines); some central nervous system depressants (including narcotics and alcohol); antihypertensive, diuretic, antihistaminic, sedative or anesthetic drugs; bupropion HCl; buspirone HCl; dextromethorphan; cheese or other foods with a high tyramine content; or excessive quantities of caffeine.

Parnate (tranylcypromine sulfate) should not be administered to any patient with a confirmed or suspected cerebrovascular defect or to any patient with cardiovascular disease, hypertension or history of headache.

(For complete discussion of contraindications and warnings, see below.)

CONTRAINDICATIONS

Parnate (tranylcypromine sulfate) is contraindicated:

1. In patients with cerebrovascular defects or cardiovascular disorders

Parnate should not be administered to any patient with a confirmed or suspected cerebrovascular defect or to any patient with cardiovascular disease or hypertension.

2. In the presence of pheochromocytoma

Parnate should not be used in the presence of pheochromocytoma since such tumors secrete pressor substances.

3. In combination with MAO inhibitors or with dibenzazepine-related entities

Parnate (tranylcypromine sulfate) should not be administered together or in rapid succession with other MAO inhibitors or with dibenzazepine-related entities. Hypertensive crises or severe convulsive seizures may occur in patients receiving such combinations.

In patients being transferred to *Parnate* from another MAO inhibitor or from a dibenzazepine-related entity, allow a medication-free interval of at least a week, then initiate *Parnate* using half the normal starting dosage for at least the first week of therapy. Similarly, at least a week should elapse between the discontinuance of *Parnate* and the administration of another MAO inhibitor or a dibenzazepine-related entity, or the readministration of *Parnate*.

The following list includes some other MAO inhibitors, dibenzazepine-related entities and tricyclic antidepressants, and the companies which market them.

Other MAO Inhibitors

Generic Name	**Source**
Furazolidone	
Isocarboxazid	Marplan® (Oxford Pharm Services)
Pargyline HCl	
Pargyline HCl and methyclothiazide	
Phenelzine sulfate	Nardil® (Parke-Davis)
Procarbazine HCl	Matulane® (Sigma Tau)

Dibenzazepine-Related and Other Tricyclics

Generic Name	**Source**
Amitriptyline HCl	Elavil® (Zeneca)
Perphenazine and amitriptyline HCl	Etrafon® (Schering)
	Triavil® (Lotus Biochemical)
Clomipramine hydrochloride	Anafranil® (Geneva)
Desipramine HCl	Norpramin® (Aventis)
Imipramine HCl	Janimine™ (Geneva)
	Tofranil® (Novartis)
Nortriptyline HCl	(Geneva)
	Pamelor® (Mallinckrodt)
Protriptyline HCl	Vivactil® (Merck & Co., Inc.)
Doxepin HCl	Sinequan® (Pfizer)
Carbamazepine	Tegretol® (Novartis)
Cyclobenzaprine HCl	Flexeril® (Merck & Co., Inc.)
Amoxapine	(Geneva)
Maprotiline HCl	(Mylan)
Trimipramine maleate	Surmontil® (Wyeth-Ayerst Pharmaceuticals)

4. In combination with bupropion

The concurrent administration of a MAO inhibitor and bupropion hydrochloride (Wellbutrin®, Wellbutrin SR®, Zyban®, GlaxoSmithKline) is contraindicated. At least 14 days should elapse between discontinuation of a MAO inhibitor and initiation of treatment with bupropion hydrochloride.

5. In combination with dexfenfluramine hydrochloride

Because dexfenfluramine hydrochloride is a serotonin releaser and reuptake inhibitor, it should not be used concomitantly with Parnate (tranylcypromine sulfate).

6. In combination with selective serotonin reuptake inhibitors (SSRIs)

As a general rule, *Parnate* should not be administered in combination with any SSRI. There have been reports of serious, sometimes fatal, reactions (including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma) in patients receiving fluoxetine (Prozac®, Eli Lilly and Company) in combination with a monoamine oxidase inhibitor (MAOI), and in patients who have recently discontinued fluoxetine and are then started on a MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Therefore, fluoxetine and other SSRIs should not be used in combination with a MAOI, or within 14 days of discontinuing therapy with a MAOI. Since fluoxetine and its major metabolite have very long elimination half-lives, at least 5 weeks should be allowed after stopping fluoxetine before starting a MAOI.

At least 2 weeks should be allowed after stopping sertraline (Zoloft®, Pfizer) or paroxetine (Paxil®, GlaxoSmithKline) before starting a MAOI.

7. In combination with buspirone

Parnate (tranylcypromine sulfate) should not be used in combination with buspirone HCl (BuSpar®, Bristol-Myers Squibb), since several cases of elevated blood pressure have been reported in patients taking MAO inhibitors who were then given buspirone HCl. At least 10 days should elapse between the discontinuation of *Parnate* and the institution of buspirone HCl.

8. In combination with sympathomimetics

Parnate (tranylcypromine sulfate) should not be administered in combination with sympathomimetics, including amphetamines, and over-the-counter drugs such as cold, hay fever or weight-reducing preparations that contain vasoconstrictors.

During *Parnate* therapy, it appears that certain patients are particularly vulnerable to the effects of sympathomimetics when the activity of certain enzymes is inhibited. Use of sympathomimetics and compounds such as guanethidine, methyldopa, reserpine, dopamine, levodopa and tryptophan with *Parnate* may precipitate hypertension, headache and related symptoms. The combination of MAOIs and tryptophan has been reported to cause behavioral and neurologic syndromes including disorientation, confusion, amnesia, delirium, agitation, hypomanic signs, ataxia, myoclonus, hyperreflexia, shivering, ocular oscillations and Babinski's signs.

9. In combination with meperidine

Do not use meperidine concomitantly with MAO inhibitors or within 2 or 3 weeks following MAOI therapy. Serious reactions have been precipitated with concomitant use, including coma, severe hypertension or hypotension, severe respiratory depression, convulsions, malignant hyperpyrexia, excitation, peripheral vascular collapse and death. It is thought that these reactions may be mediated by accumulation of 5-HT (serotonin) consequent to MAO inhibition.

10. In combination with dextromethorphan

The combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior.

11. In combination with cheese or other foods with a high tyramine content

Hypertensive crises have sometimes occurred during *Parnate* therapy after ingestion of foods with a high tyramine content. In general, the patient should avoid protein foods in which aging or protein breakdown is used to increase flavor. In particular, patients should be instructed not to take foods such as cheese (particularly strong or aged varieties), sour cream, Chianti wine, sherry, beer (including nonalcoholic beer), liqueurs, pickled herring, anchovies, caviar, liver, canned figs, dried fruits (raisins, prunes, etc.), bananas, raspberries, avocados, overripe fruit, chocolate, soy sauce, sauerkraut, the pods of broad beans (fava beans), yeast extracts, yogurt, meat extracts or meat prepared with tenderizers.

12. In patients undergoing elective surgery

Patients taking *Parnate* should not undergo elective surgery requiring general anesthesia. Also, they should not be given cocaine or local anesthesia containing sympathomimetic vasoconstrictors. The possible combined hypotensive effects of *Parnate* and spinal anesthesia should be kept in mind. *Parnate* should be discontinued at least 10 days prior to elective surgery.

ADDITIONAL CONTRAINDICATIONS

In general, the physician should bear in mind the possibility of a lowered margin of safety when Parnate (tranylcypromine sulfate) is administered in combination with potent drugs.

1. *Parnate* should not be used in combination with some central nervous system depressants such as narcotics and alcohol, or with hypotensive agents. A marked potentiating effect on these classes of drugs has been reported.

2. Anti-parkinsonism drugs should be used with caution in patients receiving *Parnate* since severe reactions have been reported.

3. *Parnate* should not be used in patients with a history of liver disease or in those with abnormal liver function tests.

4. Excessive use of caffeine in any form should be avoided in patients receiving *Parnate*.

WARNINGS TO PHYSICIANS

Clinical Worsening and Suicide Risk: Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients. Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with MDD and other psychiatric disorders.

Pooled analyses of short-term placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with MDD, OCD, or other psychiatric disorders (a total of 24

trials involving over 4,400 patients) have revealed a greater risk of adverse events representing suicidal behavior or thinking (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. There was considerable variation in risk among drugs, but a tendency toward an increase for almost all drugs studied. The risk of suicidality was most consistently observed in the MDD trials, but there were signals of risk arising from some trials in other psychiatric indications (obsessive compulsive disorder and social anxiety disorder) as well. **No suicides occurred in any of these trials.** It is unknown whether the suicidality risk in pediatric patients extends to longer-term use, i.e., beyond several months. It is also unknown whether the suicidality risk extends to adults.

All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Such observation would generally include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks of treatment, then every other week visits for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks. Additional contact by telephone may be appropriate between face-to-face visits.

Adults with MDD or co-morbid depression in the setting of other psychiatric illness being treated with antidepressants should be observed similarly for clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

In addition, patients with a history of suicidal behavior or thoughts, those patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment, and young adults, are at an increased risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Families and caregivers of pediatric patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers.

Prescriptions for *Parnate* should be written for the smallest quantity of tablets consistent with

good patient management, in order to reduce the risk of overdose. Families and caregivers of adults being treated for depression should be similarly advised.

Screening Patients for 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 may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms 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. It should be noted that *Parnate* is not approved for use in treating bipolar depression.

Parnate (tranylcypromine sulfate) is a potent agent with the capability of producing serious side effects. *Parnate* is not recommended in those depressive reactions where other antidepressant drugs may be effective. **It should be reserved for patients who can be closely supervised and who have not responded satisfactorily to the drugs more commonly administered for depression.**

Before prescribing, the physician should be completely familiar with the full material on dosage, side effects and contraindications on these pages, with the principles of MAO inhibitor therapy and the side effects of this class of drugs. Also, the physician should be familiar with the symptomatology of mental depressions and alternate methods of treatment to aid in the careful selection of patients for *Parnate* therapy.

Pregnancy Warning: Use of any drug in pregnancy, during lactation or in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to mother and child.

Animal reproductive studies show that *Parnate* passes through the placental barrier into the fetus of the rat, and into the milk of the lactating dog. The absence of a harmful action of *Parnate* on fertility or on postnatal development by either prenatal treatment or from the milk of treated animals has not been demonstrated. Tranylcypromine is excreted in human milk.

WARNING TO THE PATIENT

Patients should be instructed to report promptly the occurrence of headache or other unusual symptoms, i.e., palpitation and/or tachycardia, a sense of constriction in the throat or chest, sweating, dizziness, neck stiffness, nausea or vomiting.

Patients should be warned against eating the foods listed in Section 11 under Contraindications while on Parnate (tranylcypromine sulfate) therapy. Also, they should be told not to drink alcoholic beverages. The patient should also be warned about the possibility of hypotension and faintness, as well as drowsiness sufficient to impair performance of potentially hazardous tasks such as driving a car or operating machinery.

Patients should also be cautioned not to take concomitant medications, whether prescription or over-the-counter drugs such as cold, hay fever or weight-reducing preparations, without the advice of a physician. They should be advised not to consume excessive amounts of caffeine in any form. Likewise, they should inform other physicians, and their dentist, about their use of *Parnate*.

See PRECAUTIONS—Information for Patients for information regarding clinical worsening and suicide risk**.**

WARNINGS

HYPERTENSIVE CRISES: The most important reaction associated with Parnate (tranylcypromine sulfate) is the occurrence of hypertensive crises which have sometimes been fatal.

These crises are 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) and photophobia. Either tachycardia or bradycardia may be present, and associated constricting chest pain and dilated pupils may occur. **Intracranial bleeding, sometimes fatal in outcome, has been reported in association with the paradoxical increase in blood pressure.**

In all patients taking *Parnate* blood pressure should be followed closely 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 headaches during *Parnate* therapy. These signs may be prodromal of a hypertensive crisis.

Important:

Recommended treatment in hypertensive crises

If a hypertensive crisis occurs, Parnate (tranylcypromine sulfate) should be discontinued and therapy to lower blood pressure should be instituted immediately. Headache tends to abate as blood pressure is lowered. On the basis of present evidence, phentolamine is recommended. (The dosage reported for phentolamine is 5 mg I.V.) Care should be taken to administer this drug slowly in order 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. Do not use parenteral reserpine.

PRECAUTIONS

Hypotension

Hypotension has been observed during Parnate (tranylcypromine sulfate) therapy. Symptoms of postural hypotension are seen most commonly but not exclusively in patients with pre-existent hypertension; blood pressure usually returns rapidly to pretreatment levels upon discontinuation of the drug. At doses above 30 mg daily, postural hypotension is a major side effect and may result in syncope. Dosage increases should be made more gradually in patients showing a tendency toward hypotension at the beginning of therapy. Postural hypotension may be relieved by having the patient lie down until blood pressure returns to normal.

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.

There have been reports of drug dependency in patients using doses of tranylcypromine significantly in excess of the therapeutic range. Some of these patients had a history of previous substance abuse. The following withdrawal symptoms have been reported: restlessness, anxiety, depression, confusion, hallucinations, headache, weakness and diarrhea.

Drugs which lower the seizure threshold, including MAO inhibitors, should not be used with Amipaque®. As with other MAO inhibitors, Parnate (tranylcypromine sulfate) should be

discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.

MAO inhibitors may have the capacity to suppress anginal pain that would otherwise serve as a warning of myocardial ischemia.

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

Older patients may suffer more morbidity than younger patients during and following an episode of hypertension or malignant hyperthermia. Older patients have less compensatory reserve to cope with any serious adverse reaction. Therefore, *Parnate* should be used with caution in the elderly population.

Although excretion of *Parnate* is rapid, inhibition of MAO may persist up to 10 days following discontinuation.

Because the influence of *Parnate* on the convulsive threshold is variable in animal experiments, suitable precautions should be taken if epileptic patients are treated.

Some MAO inhibitors have contributed to hypoglycemic episodes in diabetic patients receiving insulin or oral hypoglycemic agents. Therefore, *Parnate* should be used with caution in diabetics using these drugs.

Parnate may aggravate coexisting symptoms in depression, such as anxiety and agitation.

Use Parnate (tranylcypromine sulfate) with caution in hyperthyroid patients because of their increased sensitivity to pressor amines.

Parnate should be administered with caution to patients receiving Antabuse®†. 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 (*Parnate*) and disulfiram produced no adverse interaction.

Information for Patients: Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with *Parnate* and should counsel them in its appropriate use. A patient Medication Guide About Using Antidepressants in Children and Teenagers is available for *Parnate*. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking *Parnate.*

Clinical Worsening and Suicide Risk: Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to observe for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be

associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

Pediatric Use: Safety and effectiveness in the pediatric population have not been established (see BOX WARNING and WARNINGS—Clinical Worsening and Suicide Risk). Anyone considering the use of *Parnate* in a child or adolescent must balance the potential risks with the clinical need.

ADVERSE REACTIONS

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.

Patients may experience restlessness or insomnia; may notice some weakness, drowsiness, episodes of dizziness or dry mouth; or may report nausea, diarrhea, abdominal pain or constipation. Most of these effects can be relieved by lowering the dosage or by giving suitable concomitant medication.

Tachycardia, significant anorexia, edema, palpitation, blurred vision, chills and impotence have each been reported.

Headaches without blood pressure elevation have occurred.

Rare instances of hepatitis, skin rash and alopecia have been reported.

Impaired water excretion compatible with the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) has been reported.

Tinnitus, muscle spasm, tremors, myoclonic jerks, numbness, paresthesia, urinary retention and retarded ejaculation have been reported.

Hematologic disorders including anemia, leukopenia, agranulocytosis and thrombocytopenia have been reported.

Post-Introduction Reports

The following are spontaneously reported adverse events temporally associated with *Parnate* therapy. No clear relationship between *Parnate* and these events has been established. Localized scleroderma, flare-up of cystic acne, ataxia, confusion, disorientation, memory loss, urinary frequency, urinary incontinence, urticaria, fissuring in corner of mouth, akinesia.

DOSAGE AND ADMINISTRATION

Dosage should be adjusted to the requirements of the individual patient. Improvement should be seen within 48 hours to 3 weeks after starting therapy.

The usual effective dosage is 30 mg per day, usually given in divided doses. If there are no signs of improvement after a reasonable period (up to 2 weeks), then the dosage may be increased in 10 mg per day increments at intervals of 1 to 3 weeks; the dosage range may be extended to a maximum of 60 mg per day from the usual 30 mg per day.

OVERDOSAGE

SYMPTOMS: The characteristic symptoms that may be caused by overdosage are usually those described above.

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: Gastric lavage is helpful if performed early. Treatment should normally consist of general supportive measures, close observation of vital signs and steps to counteract specific symptoms as they occur, since MAO inhibition may persist. The management of hypertensive crises is described under WARNINGS in the HYPERTENSIVE CRISES section.

External cooling is recommended if hyperpyrexia occurs. Barbiturates have been reported to help relieve myoclonic reactions, but frequency of administration should be controlled carefully because Parnate (tranylcypromine sulfate) may prolong barbiturate activity. When hypotension requires treatment, the standard measures for managing circulatory shock should be initiated. If pressor agents are used, the rate of infusion should be regulated by careful observation of the patient because an exaggerated pressor response sometimes occurs in the presence of MAO inhibition. Remember that the toxic effect of *Parnate* may be delayed or prolonged following the last dose of the drug. Therefore, the patient should be closely observed for at least a week. It is not known if tranylcypromine is dialyzable.

HOW SUPPLIED

Parnate is supplied as round, rose-red, film-coated tablets imprinted with the product name PARNATE and SB and contains tranylcypromine sulfate equivalent to 10 mg of tranylcypromine, in bottles of 100 with a desiccant, manufactured by Abbott Laboratories, North Chicago, IL 60064.

10 mg 100's: NDC 0007-4471-20

Store between 15° and 30°C (59° and 86°F).

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*metrizamide, Sanofi-Synthelabo Inc.

†disulfiram, Wyeth-Ayerst Pharmaceuticals.

Medication Guide

PARNATE® (PAR-nate) (tranylcypromine sulfate) Tablets

About Using Antidepressants in Children and Teenagers

What is the most important information I should know if my child is being prescribed an antidepressant?

Parents or guardians need to think about 4 important things when their child is prescribed an antidepressant:

1. There is a risk of suicidal thoughts or actions

2. How to try to prevent suicidal thoughts or actions in your child
3. You should watch for certain signs if your child is taking an antidepressant
4. There are benefits and risks when using antidepressants

1. There is a Risk of Suicidal Thoughts or Actions

Children and teenagers sometimes think about suicide, and many report trying to kill themselves.

Antidepressants increase suicidal thoughts and actions in some children and teenagers. But suicidal thoughts and actions can also be caused by depression, a serious medical condition that is commonly treated with antidepressants. Thinking about killing yourself or trying to kill yourself is called *suicidality* or *being suicidal.*

A large study combined the results of 24 different studies of children and teenagers with depression or other illnesses. In these studies, patients took either a placebo (sugar pill) or an antidepressant for 1 to 4 months. ***No one committed suicide in these studies,*** but some patients became suicidal. On sugar pills, 2 out of every 100 became suicidal. On the antidepressants, 4 out of every 100 patients became suicidal.

For some children and teenagers, the risks of suicidal actions may be especially high. These include patients with

- Bipolar illness (sometimes called manic-depressive illness)
- A family history of bipolar illness
- A personal or family history of attempting suicide

If any of these are present, make sure you tell your healthcare provider before your child takes an antidepressant.

2. How to Try to Prevent Suicidal Thoughts and Actions

To try to prevent suicidal thoughts and actions in your child, pay close attention to changes in her or his moods or actions, especially if the changes occur suddenly. Other important people in your child's life can help by paying attention as well (e.g., your child, brothers and sisters, teachers, and other important people). The changes to look out for are listed in Section 3, on what to watch for.

Whenever an antidepressant is started or its dose is changed, pay close attention to your child. After starting an antidepressant, your child should generally see his or her healthcare provider:

- Once a week for the first 4 weeks
- Every 2 weeks for the next 4 weeks
- After taking the antidepressant for 12 weeks

- After 12 weeks, follow your healthcare provider's advice about how often to come back
- More often if problems or questions arise (see Section 3)

You should call your child's healthcare provider between visits if needed.

3. You Should Watch for Certain Signs If Your Child is Taking an Antidepressant

Contact your child's healthcare provider ***right away*** if your child exhibits any of the following signs for the first time, or if they seem worse, or worry you, your child, or your child's teacher:

- Thoughts about suicide or dying
- Attempts to commit suicide
- New or worse depression
- New or worse anxiety
- Feeling very agitated or restless
- Panic attacks
- Difficulty sleeping (insomnia)
- New or worse irritability
- Acting aggressive, being angry, or violent
- Acting on dangerous impulses
- An extreme increase in activity and talking
- Other unusual changes in behavior or mood

Never let your child stop taking an antidepressant without first talking to his or her healthcare provider. Stopping an antidepressant suddenly can cause other symptoms.

4. There are Benefits and Risks When Using Antidepressants

Antidepressants are used to treat depression and other illnesses. Depression and other illnesses can lead to suicide. In some children and teenagers, treatment with an antidepressant increases suicidal thinking or actions. It is important to discuss all the risks of treating depression and also the risks of not treating it. You and your child should discuss all treatment choices with your healthcare provider, not just the use of antidepressants.

Other side effects can occur with antidepressants (see section below).

Of all the antidepressants, only fluoxetine (Prozac®)* has been FDA approved to treat pediatric depression.

For obsessive compulsive disorder in children and teenagers, FDA has approved only fluoxetine (Prozac®)*, sertraline (Zoloft®)*, fluvoxamine, and clomipramine (Anafranil®)*.

Your healthcare provider may suggest other antidepressants based on the past experience of your child or other family members.

Is this all I need to know if my child is being prescribed an antidepressant?

No. This is a warning about the risk for suicidality. Other side effects can occur with antidepressants. Be sure to ask your healthcare provider to explain all the side effects of the particular drug he or she is prescribing. Also ask about drugs to avoid when taking an antidepressant. Ask your healthcare provider or pharmacist where to find more information.

*The following are registered trademarks of their respective manufacturers: Prozac®/Eli Lilly and Company; Zoloft®/Pfizer Pharmaceuticals; Anafranil®/Mallinckrodt Inc.

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

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