NARDIL®
(Phenelzine Sulfate Tablets, USP)

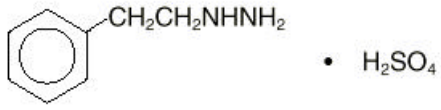
Suicidality in Children and Adolescents

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 NARDIL 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. NARDIL 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 4400 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

NARDIL® (phenelzine sulfate) is a potent inhibitor of monoamine oxidase (MAO). Phenelzine sulfate is a hydrazine derivative. It has a molecular weight of 234.27 and is chemically described as $C_8 H_{12} N_2 \bullet H_2SO_4$. Its chemical structure is shown below:



Molecular weight: 234.27

Each NARDIL film-coated tablet for oral administration contains phenelzine sulfate equivalent to 15 mg of phenelzine base and the following inactive ingredients: mannitol, USP; croscarmellose sodium, NF; povidone, USP; edetate disodium, USP; magnesium stearate, NF; isopropyl alcohol, USP; purified water, USP; opadry orange Y30-13242A; simethicone emulsion, USP.

CLINICAL PHARMACOLOGY

Monoamine oxidase is a complex enzyme system, widely distributed throughout the body. Drugs that inhibit monoamine oxidase in the laboratory are associated with a

number of clinical effects. Thus, it is unknown whether MAO inhibition per se, other pharmacologic actions, or an interaction of both is responsible for the clinical effects observed. Therefore, the physician should become familiar with all the effects produced by drugs of this class.

Pharmacokinetics

Absorption – Following a single 30 mg dose of NARDIL® (2 X 15 mg tablets), a mean peak plasma concentration (Cmax) of 19.8 ng/mL occurred at a time (Tmax) of 43 minutes postdose.

Metabolism – NARDIL® is extensively metabolized, primarily by oxidation via monoamine oxidase. After oral administration of $^{13}C_6$-phenelzine, 73% of the administered dose was recovered in urine as phenylacetic acid and parahydroxyphenylacetic acid within 96 hours. Acetylation to N^2-acetylphenelzine is a minor pathway.

Elimination – The mean elimination half-life after a single 30 mg dose is 11.6 hours. Multiple dose pharmacokinetics have not been studied in man.

INDICATIONS AND USAGE

NARDIL has been found to be effective in depressed patients clinically characterized as "atypical," "nonendogenous," or "neurotic." These patients often have mixed anxiety and depression and phobic or hypochondriacal features. There is less conclusive evidence of its usefulness with severely depressed patients with endogenous features.

NARDIL should rarely be the first antidepressant drug used. Rather, it is more suitable for use with patients who have failed to respond to the drugs more commonly used for these conditions.

CONTRAINDICATIONS

NARDIL should not be used in patients who are hypersensitive to the drug or its ingredients, with pheochromocytoma, congestive heart failure, a history of liver disease, or abnormal liver function tests.

The potentiation of sympathomimetic substances and related compounds by MAO inhibitors may result in hypertensive crises (see WARNINGS). Therefore, patients being treated with NARDIL should not take sympathomimetic drugs (including amphetamines, cocaine, methylphenidate, dopamine, epinephrine, and norepinephrine) or related compounds (including methyldopa, L-dopa, L-tryptophan, L-tyrosine, and phenylalanine). Hypertensive crises during NARDIL therapy may also be caused by the ingestion of foods with a high concentration of tyramine or dopamine. Therefore, patients being treated with NARDIL should avoid high protein food that has undergone protein breakdown by aging, fermentation, pickling, smoking, or bacterial contamination. Patients should also avoid cheeses (especially aged varieties), pickled herring, beer, wine, liver, yeast extract (including brewer's yeast in large quantities), dry sausage (including Genoa salami, hard salami, pepperoni, and Lebanon bologna), pods of broad beans (fava beans), and yogurt. Excessive amounts of caffeine and chocolate may also cause hypertensive reactions.

NARDIL should not be used in combination with dextromethorphan or with CNS depressants such as alcohol and certain narcotics. Excitation, seizures, delirium, hyperpyrexia, circulatory collapse, coma, and death have been reported in patients receiving MAOI therapy who have been given a single dose of meperidine. NARDIL should not be administered together with or in rapid succession to other MAO inhibitors because HYPERTENSIVE CRISES and convulsive seizures, fever, marked sweating, excitation, delirium, tremor, coma, and circulatory collapse may occur.

A List of MAO Inhibitors by Generic Name Follows:

pargyline hydrochloride
pargyline hydrochloride
and methylclothiazide
furazolidone
isocarboxazid
procarbazine
tranylcypromine

NARDIL should also not be used in combination with buspirone HCl, 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 NARDIL and the institution of another antidepressant or buspirone HCl, or the discontinuation of another MAO inhibitor and the institution of NARDIL.

There have been reports of serious reactions (including hyperthermia, rigidity, myoclonic movements and death) when serotoninergic drugs (e.g., dexfenfluramine, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, venlafaxine) have been combined with an MAO inhibitor. Therefore, the concomitant use of NARDIL with serotoninergic agents is contraindicated (see PRECAUTIONS-Drug Interactions). Allow at least five weeks between discontinuation of fluoxetine and initiation of NARDIL and at least 10 days between discontinuation of NARDIL and initiation of fluoxetine, or other serotoninergic agents. Before initiating NARDIL after using other serotoninergic agents, a sufficient amount of time must be allowed for clearance of the serotoninergic agent and its active metabolites.

The combination of MAO inhibitors 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 signs.

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

Patients taking NARDIL 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 NARDIL and spinal anesthesia should be kept in mind. NARDIL should be discontinued at least 10 days prior to elective surgery.

MAO inhibitors, including NARDIL, are contraindicated in patients receiving guanethidine.

WARNINGS

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 Major Depressive Disorder (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 4400 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.

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 NARDIL 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 of 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 NARDIL is not approved for use in treating bipolar depression.

It should be noted that NARDIL is not approved for use in treating any indications in the pediatric population.

The most serious reactions to NARDIL involve changes in blood pressure.

Hypertensive Crises: The most important reaction associated with NARDIL administration 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, vomiting, sweating (sometimes with fever and sometimes with cold, clammy skin),

dilated pupils, and photophobia. Either tachycardia or bradycardia may be present and can be associated with constricting chest pain.

NOTE: Intracranial bleeding has been reported in association with the increase in blood pressure.

Blood pressure should be observed frequently to detect evidence of any pressor response in all patients receiving NARDIL. Therapy should be discontinued immediately upon the occurrence of palpitation or frequent headaches during therapy.

Recommended treatment in hypertensive crisis: If a hypertensive crisis occurs, NARDIL should be discontinued immediately and therapy to lower blood pressure should be instituted immediately. On the basis of present evidence, phentolamine is recommended. (The dosage reported for phentolamine is 5 mg intravenously.) 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.

Warning to the Patient: All patients should be warned that the following foods, beverages, and medications must be avoided while taking NARDIL, and for two weeks after discontinuing use.

Foods and Beverages To Avoid

Meat and Fish
Pickled herring
Liver
Dry sausage (including Genoa salami, hard salami, pepperoni, and Lebanon bologna)

Vegetables
Broad bean pods (fava bean pods)
Sauerkraut

Dairy Products
Cheese (cottage cheese and cream cheese are allowed)
Yogurt

Beverages
Beer and wine
Alcohol-free and reduced-alcohol beer and wine products

Miscellaneous
Yeast extract (including brewer's yeast in large quantities)
Meat extract
Excessive amounts of chocolate and caffeine

Also, any spoiled or improperly refrigerated, handled, or stored protein-rich foods such as meats, fish, and dairy products, including foods that may have undergone protein changes by aging, pickling, fermentation, or smoking to improve flavor should be avoided.

OTC Medications To Avoid

Cold and cough preparations (including those containing dextromethorphan)
Nasal decongestants (tablets, drops, or spray)
Hay-fever medications

Sinus medications
Asthma inhalant medications
Antiappetite medicines
Weight-reducing preparations
“Pep” pills
L-tryptophan containing preparations

Also, certain prescription drugs should be avoided. Therefore, patients under the care of another physician or dentist should inform him/her that they are taking NARDIL.

Patients should be warned that the use of the above foods, beverages, or medications may cause a reaction characterized by headache and other serious symptoms due to a rise in blood pressure, with the exception of dextromethorphan which may cause reactions similar to those seen with meperidine. Also, there has been a report of an interaction between NARDIL and dextromethorphan (ingested as a lozenge) causing drowsiness and bizarre behavior.

Patients should be instructed to report promptly the occurrence of headache or other unusual symptoms.

Concomitant Use with Dibenzazepine Derivative Drugs

If the decision is made to administer NARDIL concurrently with other antidepressant drugs, or within less than 10 days after discontinuation of antidepressant therapy, the patient should be cautioned by the physician regarding the possibility of adverse drug interaction.

A List of Dibenzazepine Derivative Drugs by Generic Name Follows:

nortriptyline hydrochloride
amitriptyline hydrochloride
perphenazine and amitriptyline hydrochloride
clomipramine hydrochloride
desipramine hydrochloride
imipramine hydrochloride
doxepin
carbamazepine
cyclobenzaprine HCl
amoxapine
maprotiline HCl
trimipramine maleate
protriptyline HCl
mirtazapine

NARDIL should be used with caution in combination with antihypertensive drugs, including thiazide diuretics and ß-blockers, since exaggerated hypotensive effects may result.

Use in Pregnancy: The safe use of NARDIL during pregnancy or lactation has not been established. The potential benefit of this drug, if used during pregnancy, lactation, or in women of childbearing age, should be weighed against the possible hazard to the mother or fetus.

Doses of NARDIL in pregnant mice well exceeding the maximum recommended human dose have caused a significant decrease in the number of viable offspring per mouse. In addition, the growth of young dogs and rats has been retarded by doses exceeding the maximum human dose.

Use in Pediatric Patients: NARDIL is not recommended for pediatric patients under 16 years of age, since there are no controlled studies of safety in this age group. NARDIL, as with other hydrazine derivatives, has been reported to induce pulmonary and vascular tumors in an uncontrolled lifetime study in mice.

PRECAUTIONS

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 NARDIL and should counsel them in its appropriate use. A patient Medication Guide About Using Antidepressants in Children and Teenagers is available for NARDIL. 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 NARDIL.

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 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 NARDIL in a child or adolescent must balance the potential risks with the clinical need.

Nardil, as with other hydrazine derivatives, has been reported to induce pulmonary and vascular tumors in an uncontrolled lifetime study in mice.

In depressed patients, the possibility of suicide should always be considered and adequate precautions taken. It is recommended that careful observations of patients undergoing NARDIL treatment be maintained until control of depression is achieved. If necessary, additional measures (ECT, hospitalization, etc) should be instituted.

All patients undergoing treatment with NARDIL should be closely followed for symptoms of postural hypotension. Hypotensive side effects have occurred in hypertensive as well as normotensive and hypotensive patients. Blood pressure usually returns to pretreatment levels rapidly when the drug is discontinued or the dosage is reduced.

Because the effect of NARDIL on the convulsive threshold may be variable, adequate precautions should be taken when treating epileptic patients.

Of the more severe side effects that have been reported with any consistency, hypomania has been the most common. This reaction has been largely limited to patients in whom disorders characterized by hyperkinetic symptoms coexist with, but are obscured by, depressive affect; hypomania usually appeared as depression improved. If agitation is present, it may be increased with NARDIL. Hypomania and agitation have also been reported at higher than recommended doses or following long-term therapy.

NARDIL may cause excessive stimulation in schizophrenic patients; in manic-depressive states it may result in a swing from a depressive to a manic phase.

MAO inhibitors, including NARDIL, potentiate hexobarbital hypnosis in animals. Therefore, barbiturates should be given at a reduced dose with NARDIL.

MAO inhibitors inhibit the destruction of serotonin and norepinephrine, which are believed to be released from tissue stores by rauwolfia alkaloids. Accordingly, caution should be exercised when rauwolfia is used concomitantly with an MAO inhibitor, including NARDIL.

There is conflicting evidence as to whether or not MAO inhibitors affect glucose metabolism or potentiate hypoglycemic agents. This should be kept in mind if NARDIL is administered to diabetics.

Drug Interactions

In patients receiving nonselective monoamine oxidase (MAO) inhibitors in combination with serotoninergic agents (e.g., dexfenfluramine, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, venlafaxine) there have been reports of serious, sometimes fatal, reactions. Because NARDIL is a monoamine oxidase (MAO) inhibitor, NARDIL should not be used concomitantly with a serotoninergic agent (See CONTRAINDICATIONS).

Geriatric Use

Clinical studies of NARDIL did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the

elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

NARDIL is a potent inhibitor of monoamine oxidase. Because this enzyme is widely distributed throughout the body, diverse pharmacologic effects can be expected to occur. When they occur, such effects tend to be mild or moderate in severity (see below), often subside as treatment continues, and can be minimized by adjusting dosage; rarely is it necessary to institute counteracting measures or to discontinue NARDIL.

Common side effects include:

Nervous System—Dizziness, headache, drowsiness, sleep disturbances (including insomnia and hypersomnia), fatigue, weakness, tremors, twitching, myoclonic movements, hyperreflexia.

*Gastrointestina*l—Constipation, dry mouth, gastrointestinal disturbances, elevated serum transaminases (without accompanying signs and symptoms).

Metabolic—Weight gain.

Cardiovascular—Postural hypotension, edema.

Genitourinary—Sexual disturbances, eg, anorgasmia and ejaculatory disturbances and impotence.

Less common mild to moderate side effects (some of which have been reported in a single patient or by a single physician) include:

Nervous System—Jitteriness, palilalia, euphoria, nystagmus, paresthesias.

Genitourinary—Urinary retention.

Metabolic—Hypernatremia.

Dermatologic—Pruritus, skin rash, sweating.

Special Senses—Blurred vision, glaucoma.

Although reported less frequently, and sometimes only once, additional severe side effects include:

Nervous System—Ataxia, shock-like coma, toxic delirium, manic reaction, convulsions, acute anxiety reaction, precipitation of schizophrenia, transient respiratory and cardiovascular depression following ECT.

Gastrointestinal—To date, fatal progressive necrotizing hepatocellular damage has been reported in very few patients. Reversible jaundice.

Hematologic—Leukopenia.

Immunologic—Lupus-like syndrome

Metabolic—Hypermetabolic syndrome (which may include, but is not limited to, hyperpyrexia, tachycardia, tachypnea, muscular rigidity, elevated CK levels, metabolic acidosis, hypoxia, coma and may resemble an overdose).

Respiratory—Edema of the glottis.

General—Fever associated with increased muscle tone.

Withdrawal may be associated with nausea, vomiting, and malaise.

An uncommon withdrawal syndrome following abrupt withdrawal of NARDIL has been infrequently reported. Signs and symptoms of this syndrome generally commence 24 to 72 hours after drug discontinuation and may range from vivid nightmares with agitation to frank psychosis and convulsions. This syndrome generally responds to reinstitution of low-dose NARDIL therapy followed by cautious downward titration and discontinuation.

DOSAGE AND ADMINISTRATION

Initial dose: The usual starting dose of NARDIL is one tablet (15 mg) three times a day.

Early phase treatment: Dosage should be increased to at least 60 mg per day at a fairly rapid pace consistent with patient tolerance. It may be necessary to increase dosage up to 90 mg per day to obtain sufficient MAO inhibition. Many patients do not show a clinical response until treatment at 60 mg has been continued for at least 4 weeks.

Maintenance dose: After maximum benefit from NARDIL is achieved, dosage should be reduced slowly over several weeks. Maintenance dose may be as low as one tablet, 15 mg, a day or every other day, and should be continued for as long as is required.

OVERDOSAGE

Note—For management of *hypertensive crises* see WARNINGS section.

Accidental or intentional overdosage may be more common in patients who are depressed. It should be remembered that multiple drugs and/or alcohol may have been ingested.

Depending on the amount of overdosage with NARDIL, a varying and mixed clinical picture may develop, including signs and symptoms of central nervous system and cardiovascular stimulation and/or depression. Signs and symptoms may be absent or minimal during the initial 12-hour period following ingestion and may develop slowly thereafter, reaching a maximum in 24-48 hours. Death has been reported following overdosage. Therefore, immediate hospitalization, with continuous patient observation and monitoring throughout this period, is essential.

Signs and symptoms of overdosage may include, alone or in combination, any of the following: drowsiness, dizziness, faintness, irritability, hyperactivity, agitation, severe headache, hallucinations, trismus, opisthotonus, rigidity, convulsions, and coma; rapid and irregular pulse, hypertension, hypotension, and vascular collapse; precordial pain, respiratory depression and failure, hyperpyrexia, diaphoresis, and cool, clammy skin.

Treatment

Intensive symptomatic and supportive treatment may be required. Induction of emesis or gastric lavage with instillation of charcoal slurry may be helpful in early poisoning,

provided the airway has been protected against aspiration. Signs and symptoms of central nervous system stimulation, including convulsions, should be treated with diazepam, given slowly intravenously. Phenothiazine derivatives and central nervous system stimulants should be avoided. Hypotension and vascular collapse should be treated with intravenous fluids and, if necessary, blood pressure titration with an intravenous infusion of dilute pressor agent. It should be noted that adrenergic agents may produce a markedly increased pressor response.

Respiration should be supported by appropriate measures, including management of the airway, use of supplemental oxygen, and mechanical ventilatory assistance, as required.

Body temperature should be monitored closely. Intensive management of hyperpyrexia may be required. Maintenance of fluid and electrolyte balance is essential.

There are no data on the lethal dose in man. The pathophysiologic effects of massive overdosage may persist for several days, since the drug acts by inhibiting physiologic enzyme systems. With symptomatic and supportive measures, recovery from *mild* overdosage may be expected within 3 to 4 days.

Hemodialysis, peritoneal dialysis, and charcoal hemoperfusion may be of value in massive overdosage, but sufficient data are not available to recommend their routine use in these cases.

Toxic blood levels of phenelzine have not been established, and assay methods are not practical for clinical or toxicological use.

HOW SUPPLIED

Each NARDIL tablet is orange, biconvex, film-coated, and engraved with “P-D 270” and contains phenelzine sulfate equivalent to 15 mg of phenelzine base.

NDC 0071-0350-24. Bottle of 100

Storage:
Store between 15° - 30°C (59° - 86°F).

REFERENCES

1. Study 902-21: A Single-Dose Bioequivalence Study in Healthy Subjects Comparing a New Color-Coated Formulation of 15-mg Phenelzine Sulfate Tablets [Angers] to Currently Marketed Nardil Tablets [Lititz].
2. GB Baker, LJ Urichuk, KF McKenna and SH Kennedy. Metabolism of Monoamine Oxidase Inhibitors. Cellular and Molecular Neurobiology, Vol. 19, No. 3, 1999, pp. 411-426.
3. Donald S. Robinson, et al. Metabolism and Pharmacokinetics of Phenelzine: Lack of evidence for Acetylation Pathway in Humans. Journal of Clinical Psychopharmacology, Vol. 5, No. 6, 1985, pp. 333-337.
4. Donald S. Robinson, et al. Clinical Pharmacology of Phenelzine. Arch Gen Psychiatry, Vol 35, May 1978, pp. 629-635.

Rx only

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Medication Guide
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.

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