MAPROTILINE HYDROCHLORIDE TABLETS, USP
25 mg, 50 mg and 75 mg

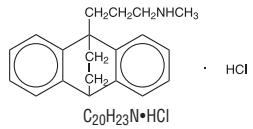
℞ only

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of maprotiline or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and 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. Maprotiline is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients and PRECAUTIONS: Pediatric Use.)

MAP:R14mc

DESCRIPTION: Maprotiline hydrochloride, USP is a tetracyclic antidepressant, available as 25 mg, 50 mg and 75 mg tablets for oral administration. Its chemical name is N-methyl-9,10-ethanoanthracene-9(10H)-propylamine hydrochloride, and its structural formula is:



$C_{20}H_{23}N{\bullet}HCl$

Maprotiline hydrochloride is a fine, white to off-white, practically odorless crystalline powder. It is freely soluble in methanol and in chloroform, slightly soluble in water, and practically insoluble in isooctane. Its molecular weight is 313.87.

The tablets contain the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hypromellose, magnesium stearate, microcrystalline cellulose, polydextrose, polyethylene glycol, pregelatinized starch (corn), sodium lauryl sulfate, titanium dioxide and triacetin. Additionally, the 50 mg tablet contains FD&C Blue No. 1 Aluminum Lake.

CLINICAL PHARMACOLOGY: The mechanism of action of maprotiline is not precisely known. It does not act primarily by stimulation of the central nervous system and is not a monoamine oxidase inhibitor. The postulated mechanism of maprotiline is that it acts primarily by potentiation of central adrenergic synapses by blocking reuptake of norepinephrine at nerve endings. This pharmacologic action is thought to be responsible for the drug's antidepressant and anxiolytic effects.

The mean time to peak is 12 hours. The half-life of elimination averages 51 hours.

Steady-state levels measured prior to the morning dose on a one dosage regimen are summarized as follows:

Regimen	Average Minimum Concentration ng/mL	95% Confidence Limits ng/mL
50 mg x 3 daily	238	181-295

INDICATIONS AND USAGE: Maprotiline hydrochloride tablets are indicated for the treatment of depressive illness in patients with depressive neurosis (dysthymic disorder) and manic depressive illness, depressed type (major depressive disorder). Maprotiline is also effective for the relief of anxiety associated with depression.

CONTRAINDICATIONS: Maprotiline hydrochloride tablets are contraindicated in patients hypersensitive to maprotiline and in patients with known or suspected seizure disorders. It should not be given concomitantly with monoamine oxidase (MAO) inhibitors. A minimum of 14 days should be allowed to elapse after discontinuation of MAO inhibitors before treatment with maprotiline is initiated. Effects should be monitored with gradual increase in dosage until optimum response is achieved. The drug is not recommended for use during the acute phase of myocardial infarction.

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. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18 to 24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1,000 patients treated) are provided in Table 1.

Table 1:

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality Per 1,000 Patients Treated
Increases Compared to Placebo	
< 18	14 additional cases
18 to 24	5 additional cases
Decreases Compared to Placebo	
25 to 64	1 fewer case
≥ 65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide.

It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression.

All patients being treated with antidepressants for any indication should be monitored appropriately and 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.

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 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 healthcare providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for maprotiline should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

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 maprotiline is not approved for use in treating bipolar depression.

Seizures have been associated with the use of maprotiline. Most of the seizures have occurred in patients without a known history of seizures. However, in some of these cases, other confounding factors were present, including concomitant medications known to lower the seizure threshold, rapid escalation of the dosage of maprotiline, and dosage that exceeded the recommended therapeutic range. The incidence of direct reports is less than 1/10 of 1%. The risk of seizures may be increased when maprotiline is taken concomitantly with phenothiazines, when the dosage of benzodiazepines is rapidly tapered in patients receiving maprotiline or when the recommended dosage of maprotiline hydrochloride is exceeded. While a cause and effect relationship has not been established, the risk of seizures in patients treated with maprotiline may be reduced by (1) initiating therapy at a low dosage, (2) maintaining the initial dosage for 2 weeks before raising it gradually in small increments as necessitated by the long half-life of maprotiline (average 51 hours), and (3) keeping the dosage at the minimally effective level during maintenance therapy. (See DOSAGE AND ADMINISTRATION.)

Extreme caution should be used when this drug is given to:

— patients with a history of myocardial infarction;

— patients with a history or presence of cardiovascular disease because of the possibility of conduction defects, arrhythmias, myocardial infarction, strokes and tachycardia.

Angle-Closure Glaucoma: The pupillary dilation that occurs following use of many antidepressant drugs including maprotiline may trigger an angle-closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

PRECAUTIONS: General: The possibility of suicide in seriously depressed patients is inherent in their illness and may persist until significant remission occurs. Therefore, patients must be carefully supervised during all phases of treatment with maprotiline, and prescriptions should be written for the smallest number of tablets consistent with good patient management.

Hypomanic or manic episodes have been known to occur in some patients taking tricyclic antidepressant drugs, particularly in patients with cyclic disorders. Such occurrences have also been noted, rarely, with maprotiline.

Prior to elective surgery, maprotiline should be discontinued for as long as clinically feasible, since little is known about the interaction between maprotiline and general anesthetics.

Maprotiline should be administered with caution in patients with history of urinary retention, or history of narrow angle glaucoma because of the drug's anticholinergic properties.

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 maprotiline and should counsel them in its appropriate use. A patient Medication Guide about "Antidepressant Medicines, Depression and other Serious Mental Illness and Suicidal Thoughts or Actions" is available for maprotiline. 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 maprotiline.

Patients should be advised that taking maprotiline can cause mild pupillary dilation, which in susceptible individuals, can lead to an episode of angle-closure glaucoma. Pre-existing glaucoma is almost always open-angle glaucoma because angle-closure glaucoma, when diagnosed, can be treated definitively with iridectomy. Open-angle glaucoma is not a risk factor for angle-closure glaucoma. Patients may wish to be examined to determine whether they are susceptible to angle-closure, and have a prophylactic procedure (e.g., iridectomy), if they are susceptible.

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 look 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.

Laboratory Tests: Maprotiline should be discontinued if there is evidence of pathological neutrophil depression. Leukocyte and differential counts should be performed in patients who develop fever and sore throat during therapy.

Drug Interactions: Close supervision and careful adjustment of dosage are required when administering maprotiline concomitantly with anticholinergic or sympathomimetic drugs because of the possibility of additive atropine like effects.

Concurrent administration of maprotiline with electroshock therapy should be avoided because of the lack of experience in this area.

Caution should be exercised when administering maprotiline to hyperthyroid patients or those on thyroid medication because of the possibility of enhanced potential for cardiovascular toxicity of maprotiline.

Maprotiline should be used with caution in patients receiving guanethidine or similar agents since it may block the pharmacologic effects of these drugs.

The risk of seizures may be increased when maprotiline is taken concomitantly with phenothiazines or when the dosage of benzodiazepines is rapidly tapered in patients receiving maprotiline.

Because of the pharmacologic similarity of maprotiline hydrochloride to the tricyclic antidepressants, the plasma concentration of maprotiline may be increased when the drug is given concomitantly with hepatic enzyme inhibitors (e.g., cimetidine, fluoxetine) and decreased by concomitant administration with hepatic enzyme inducers (e.g., barbiturates, phenytoin), as has occurred with tricyclic antidepressants. Adjustment of the dosage of maprotiline hydrochloride may therefore be necessary in such cases.

(See PRECAUTIONS: Information for Patients.)

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity and chronic toxicity studies have been conducted in laboratory rats and dogs. No drug- or dose-related occurrence of carcinogenesis was evident in rats receiving daily oral doses up to 60 mg/kg of maprotiline hydrochloride for 18 months or in dogs receiving daily oral doses up to 30 mg/kg of maprotiline hydrochloride for one year. In addition, no evidence of mutagenic activity was found in offspring of female mice mated with males treated with up to 60 times the maximum daily human dose.

Pregnancy: ***Teratogenic Effects. Pregnancy Category B:*** Reproduction studies have been performed in female laboratory rabbits, mice, and rats at doses up to 1.3, 7, and 9 times the maximum daily human dose respectively and have revealed no evidence of impaired fertility or harm to the fetus due to maprotiline. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery: Although the effect of maprotiline on labor and delivery is unknown, caution should be exercised as with any drug with CNS depressant action.

Nursing Mothers: Maprotiline is excreted in breast milk. At steady-state, the concentrations in milk correspond closely to the concentrations in whole blood. Caution should be exercised when maprotiline hydrochloride is administered to a nursing woman.

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

ADVERSE REACTIONS: The following adverse reactions have been noted with maprotiline and are generally similar to those observed with tricyclic antidepressants.

Cardiovascular: Rare occurrences of hypotension, hypertension, tachycardia, palpitation, arrhythmia, heart block, and syncope have been reported with maprotiline.

Psychiatric: Nervousness (6%), anxiety (3%), insomnia (2%), and agitation (2%); rarely, confusional states (especially in the elderly), hallucinations, disorientation, delusions, restlessness, nightmares, hypomania, mania, exacerbation of psychosis, decrease in memory, and feelings of unreality.

Neurological: Drowsiness (16%), dizziness (8%), tremor (3%), and, rarely, numbness, tingling, motor hyperactivity, akathisia, seizures, EEG alterations, tinnitus, extrapyramidal symptoms, ataxia, and dysarthria.

Anticholinergic: Dry mouth (22%), constipation (6%), and blurred vision (4%); rarely, accommodation disturbances, mydriasis, urinary retention, and delayed micturition.

Allergic: Rare instances of skin rash, petechiae, itching, photosensitization, edema, and drug fever.

Gastrointestinal: Nausea (2%) and, rarely, vomiting, epigastric distress, diarrhea, bitter taste, abdominal cramps and dysphagia.

Endocrine: Rare instances of increased or decreased libido, impotence, and elevation or depression of blood sugar levels.

Other: Weakness and fatigue (4%) and headache (4%); rarely, altered liver function, jaundice, weight loss or gain, excessive perspiration, flushing, urinary frequency, increased salivation, nasal congestion and alopecia.

Note: Although there have been only isolated reports of the following adverse reactions with maprotiline, its pharmacologic similarity to tricyclic antidepressants requires that each reaction be considered when administering maprotiline.

— Bone marrow depression, including agranulocytosis, eosinophilia, purpura, and thrombocytopenia, myocardial infarction, stroke, peripheral neuropathy, sublingual adenitis, black tongue, stomatitis, paralytic ileus, gynecomastia in the male, breast enlargement and galactorrhea in the female, and testicular swelling.

Postintroduction Reports: Voluntary reports of adverse events temporally associated with maprotiline that have been received since market introduction and that may have no casual relationship with the drug include the following: interstitial pneumonitis which were in some cases associated with eosinophilia and increased liver enzymes, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis.

OVERDOSAGE: Deaths may occur from overdosage with this class of drugs. Multiple drug ingestion (including alcohol) is common in deliberate overdose. As the management is complex and changing, it is recommended that the physician contact a poison control center for current information on treatment. Signs and symptoms of toxicity develop rapidly after overdose. Therefore, hospital monitoring is required as soon as possible.

Animal Oral LD_{50}: The oral LD_{50} of maprotiline hydrochloride is 600 to 750 mg/kg in mice, 760 to 900 mg/kg in rats, > 1000 mg/kg in rabbits, > 300 mg/kg in cats, and > 30 mg/kg in dogs.

Manifestations: Data dealing with overdosage in humans are limited with only a few cases on record. Signs and symptoms of maprotiline hydrochloride overdose are similar to those seen with tricyclic overdose. Critical manifestations of overdose include cardiac dysrhythmias, severe hypotension, convulsions and CNS depression including coma. Changes in the electrocardiogram, particularly in QRS axis or width are clinically significant indicators of toxicity. Other clinical manifestations include drowsiness, tachycardia, ataxia, vomiting, cyanosis, shock, restlessness, agitation, hyperpyrexia, muscle rigidity, athetoid movements, and mydriasis. Since congestive heart failure has been seen with overdosages of tricyclic antidepressants, it should be considered with maprotiline hydrochloride overdosage.

Management: Obtain an ECG and immediately initiate cardiac monitoring. Protect the patient's airway, establish an intravenous line and initiate gastric decontamination. A minimum of 6 hours of observation with cardiac monitoring and observation for signs of CNS or respiratory depression, hypotension, cardiac dysrhythmias and/or conduction blocks, and seizures is necessary. If signs of toxicity occur at any time during this period, extended monitoring is required. There are case reports of patients succumbing to fatal dysrhythmias late after tricyclic overdose; these patients had clinical evidence of significant poisoning prior to death and most received inadequate gastrointestinal decontamination. Monitoring of plasma drug levels should not guide management of the patient.

Gastrointestinal Decontamination: All patients suspected of overdose should receive gastrointestinal decontamination. This should include large volume gastric lavage followed by activated charcoal. If consciousness is impaired, the airway should be secured prior to lavage. Emesis is contraindicated.

Cardiovascular: A maximal limb lead QRS duration of ≥ 0.10 seconds may be the best indication of the severity of the overdose. Intravenous sodium bicarbonate should be used to maintain the serum pH in the range of 7.45 to 7.55. If the pH response is inadequate, hyperventilation may also be used. Concomitant use of hyperventilation and sodium bicarbonate should be done with extreme caution, with frequent pH monitoring. A pH > 7.60 or a Pco_2 < 20 mmHg is undesirable. Dysrhythmias unresponsive to sodium bicarbonate therapy/hyperventilation may respond to lidocaine, bretylium, or phenytoin. Type 1A and 1C antiarrhythmics are generally contraindicated (e.g., quinidine, disopyramide, and procainamide).

In rare instances, hemoperfusion may be beneficial in acute refractory cardiovascular instability in patients with acute toxicity. However, hemodialysis, peritoneal dialysis, exchange transfusions, and forced diuresis generally have been reported as ineffective.

CNS: In patients with CNS depression, early intubation is advised because of the potential for abrupt deterioration. Seizures should be controlled with benzodiazepines, or if these are ineffective, other anticonvulsants (e.g., phenobarbital, phenytoin). Physostigmine is not recommended except to treat life threatening symptoms that have been unresponsive to other therapies, and then only in consultation with a poison control center.

Psychiatric Follow-up: Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Psychiatric referral may be appropriate.

Pediatric Management: The principles of management of child and adult overdosages are similar. It is strongly recommended that the physician contact the local poison control center for specific pediatric treatment.

DOSAGE AND ADMINISTRATION: A single daily dose is an alternative to divided daily doses. Therapeutic effects are sometimes seen within 3 to 7 days, although as long as 2 to 3 weeks are usually necessary.

Initial Adult Dosage: An initial dosage of 75 mg daily is suggested for outpatients with mild to moderate depression. However, in some patients, particularly the elderly, an initial dosage of 25 mg daily may be used. Because of the long half-life of maprotiline, the initial dosage should be maintained for 2 weeks. The dosage may then be increased gradually in 25 mg increments as required and tolerated. In most outpatients a maximum dose of 150 mg daily will result in therapeutic efficacy. It is recommended that this dose not be exceeded except in the most severely depressed patients. In such patients, dosage may be gradually increased to a maximum of 225 mg.

More severely depressed, hospitalized patients should be given an initial daily dose of 100 mg to 150 mg which may be gradually increased as required and tolerated. Most hospitalized patients with moderate to severe depression respond to a daily dose of 150 mg although dosages as high as 225 mg may be required in some cases. Daily dosage of 225 mg should not be exceeded.

Elderly Patients: In general, lower dosages are recommended for patients over 60 years of age. Dosages of 50 mg to 75 mg daily are usually satisfactory as maintenance therapy for elderly patients who do not tolerate higher amounts.

Maintenance: Dosage during prolonged maintenance therapy should be kept at the lowest effective level. Dosage may be reduced to levels of 75 mg to 150 mg daily during such periods, with subsequent adjustment depending on therapeutic response.

HOW SUPPLIED: Maprotiline Hydrochloride, USP is available as tablets containing 25 mg, 50 mg, or 75 mg of maprotiline hydrochloride.

The 25 mg tablets are white film-coated, round, scored tablets debossed with **6** to the left of the score and **0** to the right of the score on one side of the tablet and **M** on the other side. They are available as follows:

NDC 0378-0060-01
bottles of 100 tablets

The 50 mg tablets are light blue film-coated, round, scored, tablets debossed with **8** to the left of the score and **7** to the right of the score on one side and **M** on the other side. They are available as follows:

NDC 0378-0087-01
bottles of 100 tablets

The 75 mg tablets are white film-coated, round, scored tablets debossed with **9** to the left of the score and **2** to the right of the score on one side and **M** on the other side. They are available as follows:

NDC 0378-0092-01
bottles of 100 tablets

Store at 20° to 25°C (68° to 77°F). [See USP for Controlled Room Temperature.]
Protect from light.

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

PHARMACIST: Dispense a Medication Guide with each prescription.

Mylan®

Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

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MAP:R14mc

Medication Guide

Antidepressant Medicines, Depression and other Serious Mental Illnesses, and Suicidal Thoughts or Actions

Read the Medication Guide that comes with you or your family member's antidepressant medicine. This Medication Guide is only about the risk of suicidal thoughts and actions with antidepressant medicines. **Talk to your, or your family member's, healthcare provider about:**

- all risks and benefits of treatment with antidepressant medicines
- all treatment choices for depression or other serious mental illness

What is the most important information I should know about antidepressant medicines, depression and other serious mental illnesses, and suicidal thoughts or actions?

1. **Antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment.**
2. **Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a particularly high risk of having suicidal thoughts or actions.** These include people who have (or have a family history of) bipolar illness also called manic-depressive illness) or suicidal thoughts or actions.
3. **How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?**
   - Pay close attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed.
   - Call the healthcare provider right away to report new or sudden changes in mood, behavior, thoughts, or feelings.
   - Keep all follow-up visits with the healthcare provider as scheduled. Call the healthcare provider between visits as needed, especially if you have concerns about symptoms.

Call a healthcare provider right away if you or your family member has any of the following symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling very agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood
- **visual problems:** eye pain, changes in vision, swelling or redness in or around the eye.

What else do I need to know about antidepressant medicines?

- **Never stop an antidepressant medicine without first talking to a healthcare provider.** Stopping an antidepressant medicine suddenly can cause other symptoms.
- **Visual problems:** Only some people are at risk for these problems. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are.
- **Antidepressants are medicines used to treat depression and other illnesses.** It is important to discuss all the risks of treating depression and also the risks of not treating it. Patients and their families or other caregivers should discuss all treatment choices with the healthcare provider, not just the use of antidepressants.
- **Antidepressant medicines have other side effects.** Talk to the healthcare provider about the side effects of the medicine prescribed for you or your family member.
- **Antidepressant medicines can interact with other medicines.** Know all of the medicines that you or your family member takes. Keep a list of all medicines to show the healthcare provider. Do not start new medicines without first checking with your healthcare provider.
- **Not all antidepressant medicines prescribed for children are FDA approved for use in children.** Talk to your child's healthcare provider for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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

Revised 5/2014