Significant mention occurs. Suicide is a known risk of depression and certain other psychotropic 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 the increased rate of worsening depression and suicide attempts in certain patients during the early phases of treatment. Pool analyses of short-term placebo-controlled trials of antidepressants indicated that patients who had previously experienced suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or other changes are made, or who are discontinuing the medication, are at increased risk of suicide. Families and caregivers of patients should be advised to report any 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 abrupt or if the patient is tending to withdraw from social interaction. The presence of such symptoms should be reported to the prescriber or health professional immediately. 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.

Patients should be advised that taking doxepin capsules can cause mild ptyalism, which is a possible side effect. This effect is known to be dose-related and may be further reduced by the addition of saliva-stimulating medications to the treatment regimen. Patients should be instructed to consult their healthcare provider if this effect becomes troublesome.

Doxepin capsules should be used cautiously in patients with recently altered fluid and electrolyte balance, including patients with ascites, cerebral arteriosclerosis, high fever, polyuria, or dehydration. Patients should be instructed to consult their healthcare provider if they experience a change in fluid or electrolyte balance.

Patients should be instructed to take doxepin at the same time of day and to avoid taking doxepin with grapefruit juice or grapefruit. Patients should be instructed to consult their healthcare provider if they experience any change in the amount of fluid they drink.

Doxepin capsules should be used cautiously in patients with recent changes in cardiac conduction, including patients with signs or symptoms of heart block, conduction disturbances, increased atrioventricular block, and sick sinus syndrome. Patients should be instructed to consult their healthcare provider if they experience any change in cardiac conduction.

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generally should be started at low doses of drugs and observed closely. (See WARNINGS.)

ADVERSE REACTIONS: NOTE: Some of the adverse reactions noted below have not been specifically reported with doxepin use. However, due to the close pharmacological similarities among the tetracyclics, the reactions should be considered when prescribing doxepin.

Anticholinergic Effects: Dry mouth, blurred vision, constipation and urinary retention have been reported. If they do not subside with continued therapy or become severe, it may be necessary to reduce the dosage.

Central Nervous System Effects: Dreams are the most commonly noted side effect. This tends to disappear as therapy is continued. Other commonly reported CNS side effects are confusion, disorientation, hallucinations, numbness, paresthesias, ataxia, extrapyramidal symptoms, seizures, tardive dyskinesia and tremor.

Cardiovascular: Cardiovascular effects including hypertension, tachycardia and tachyarrhythmias have been reported occasionally.

Allergic: Skin rash, urticaria, photosensitivity and pruritis have occasionally occurred.

Hematologic: Eosinophilia has been reported in a few patients. There have been occasional reports of bone marrow depression manifesting as aplastic anemia, leukopenia, thrombocytopenia and purpura.

Gastrointestinal: Nausea, vomiting, indigestion, taste disturbances, diarrhea, anorexia and aphthous stomatitis have been reported. (See Anticholinergic Effects.)

Endocrine: Racem and or lowered libido, breast tenderness, gynecomastia in males, enlargement of breasts and galactorrhea in the female, raising or lowering of blood sugar levels and symptoms of inappropriate antidiuretic hormone secretion have been reported with tetracyclic antidepressants.

Other: Dizziness, tinnitus, weight gain, sweating, chills, fatigue, weakness, flushing, jaundice, alopecia, headache, exacerbation of asthma and hyperactivity in association with chlorpromazine have been occasionally observed as adverse effects.

Withdrawal Symptoms: The possibility of development of withdrawal symptoms upon abrupt cessation of treatment after prolonged doxepin administration should be borne in mind. These are not indicative of addiction and gradual withdrawal of medication should not cause these symptoms.

OVERDOSAGE: Deaths may occur from overdosage with this class of drugs. Multiple drug ingestion (including alcohol) is common in deliberate tricyclic antidepressant overdosage. 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 tricyclic antidepressant overdose; therefore, hospital monitoring is required as soon as possible.

Manifestations: Critical manifestations of overdose include: cardiac dysrhythmias, severe hypotension, convulsions and CNS depression, including coma. Changes in the electrocardiogram, particularly in QRS a-w or a-w, are clinically significant indicators of tetracyclic antidepressant toxicity.

Other signs of overdose may include confusion, disturbed concentration, transient visual hallucinations, dilated pupils, agitation, hyperactive reflexes, stupor, diarrhea, muscular rigidity, vomiting, psychosis, hyperreflexia, or any of the symptoms listed under ADVERSE REACTIONS.

Deaths have been reported involving overdoses of doxepin.

General Recommendations: General: 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 strongly advised. If signs of toxicity occur at any time during this period, extended monitoring is recommended. There are case reports of patients surviving to fatal dysrhythmias late after overdosage; 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 Recontamination: All patients suspected of tricyclic antidepressant 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. Emetics is contraindicated.

Cardiovascular: A maximal limit of 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 7.40 to 7.55. If the pH response is inadequate, or if hypernatremia also occurs, sodium bicarbonate should be used with extreme caution, with frequent pH monitoring. A pH of 7.40 or a pCO2 of 20 mm Hg is undesirable. Dysthenin suspense to sodium bicarbonate therapy/hypernatremia may respond to lidocaine, bretylium or phenytoin. Type IA and IC antiarrhythmics are generally contraindicated (e.g., quinidine, disopyramide and procaainamide).

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 in tricyclic antidepressant poisoning.

CNS: In patients with CNS depression, intubation and ventilation 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). Phenytoin 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.

DOSEAGE AND ADMINISTRATION: For most patients with illness of mild to moderate severity, a starting daily dose of 75 mg is recommended. Dosage may subsequently be increased or decreased at 10 mg increments. Your doctor may use the dosage between 1.5 mg/kg/day to 5 mg/kg/day.

In more severely ill patients higher doses may be required with subsequent gradual increase to 300 mg/day if necessary. Additional therapeutic effect is rarely to be obtained by exceeding a dose of 300 mg/day.

In patients with very mild symptoms/affective disorder or emotional symptoms accompanying organic disease, lower doses may suffice. Some of these patients have been controlled on doses as low as 25 to 50 mg/day.

The total daily dosage of doxepin (as the hydrochloride) may be given on a divided or once a day dosage schedule. If the once a day schedule is employed the maximum recommended dose is 250 mg/day. This dose may be given at bedtime. The 150 mg capsule strength is intended for maintenance therapy only and is not recommended for initiation of treatment.

Antipsychotic effect appears to be apparent before the antidepressant effect. Optimal antidepressant effect may not be evident for 2 to 3 weeks.

How Supplied: Doxepin Hydrochloride Capsules, USP are available containing doxepin hydrochloride, USP equivalent to 10 mg, 25 mg, 50 mg, 75 mg or 100 mg of doxepin.

The 10 mg capsule is a hard-shell, gelatin capsule with a buff opaque cap and buff opaque body sealed with hypromellose. The capsule body is black in color.

The 25 mg capsule is a hard-shell, gelatin capsule with an iridescent opaque white cap and white opaque body sealed with hypromellose. The capsule body is black in color.

The 50 mg capsule is a hard-shell, gelatin capsule with an iridescent opaque white cap and white opaque body sealed with hypromellose. The capsule body is black in color.

The 75 mg capsule is a hard-shell, gelatin capsule with a blue or green opaque cap and blue opaque body sealed with hypromellose. The capsule body is black in color.

The 100 mg capsule is a hard-shell, gelatin capsule with a blue or green opaque cap and blue opaque body sealed with hypromellose. The capsule body is black in color.

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.

Pharmacists: Dispense a Medication Guide with each prescription.

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Medication Guide
Antidepressant Medicines, Depression and Other Serious Mental Illnesses, and Suicidal Thoughts or Actions

Read the Medication Guide that comes with your 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 or trouble 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 aggressively, 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.

• Visusal 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.