selective serotonin-reuptake inhibitors may be preferred in patients in whom certain adverse GI effects (e.g., nausea, anorexia), nervous system effects (e.g., anxiety, nervousness, insomnia), and/or weight loss are not tolerated or are of concern, since such effects appear to occur more frequently with citalopram and other drugs in this class.

Pediatric Considerations. The clinical presentation of depression in children and adolescents† can differ from that in adults and generally varies with the age and developmental stages of the child. Younger children may exhibit behavioral problems such as social withdrawal, aggressive behavior, apathy, sleep disruption, and weight loss; adolescents may present with somatic complaints, self-esteem problems, rebelliousness, poor performance in school, or a pattern of engaging in risky or aggressive behavior.

Only limited data are available to date from controlled clinical studies evaluating various antidepressant agents in children and adolescents, and many of these studies have methodologic limitations (e.g., nonrandomized or uncontrolled, small sample size, short duration, nonspecific inclusion criteria). However, there is some evidence that the response to antidepressants in pediatric patients may differ from that seen in adults, and caution should be used in extrapolating data from adult studies when making treatment decisions for pediatric patients.

Results of several studies evaluating tricyclic antidepressants (e.g., amitriptyline, desipramine, imipramine, nortriptyline) in preadolescent and adolescent patients with major depression indicate a lack of overall efficacy in this age group. Based on the lack of efficacy data regarding use of tricyclic antidepressants and MAO inhibitors in pediatric patients and because of the potential for life-threatening adverse effects associated with the use of these drugs, many experts consider selective serotonin-reuptake inhibitors, including citalopram, the drugs of choice when antidepressant therapy is indicated for the treatment of major depressive disorder in children and adolescents. However, the US Food and Drug Administration (FDA) states that, while efficacy of fluoxetine has been established in pediatric patients, efficacy of other newer antidepressants (i.e., citalopram, duloxetine, escitalopram, fluvoxamine, mirtazapine, nefazodone, paroxetine, sertraline, venlafaxine) was not conclusively established in clinical trials in pediatric patients with major depressive disorder. In addition, FDA now warns that antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder and other psychiatric disorders. (See Cautions: Pediatric Precautions.) FDA currently states that anyone considering using an antidepressant in a child or adolescent for any clinical use must balance the potential risk of therapy with the clinical need. (See Cautions: Precautions and Contraindications.)

Geriatric Considerations. The response to antidepressants in geriatric patients is similar to that reported in younger adults, but depression in geriatric patients often is not recognized and is not treated. In geriatric patients with major depressive disorder, selective serotonin-reuptake inhibitors appear to be as effective as tricyclic antidepressants but may cause fewer overall adverse effects than these other agents. Geriatric patients appear to be especially sensitive to anticholinergic (e.g., dry mouth, constipation, vision disturbance), cardiovascular, orthostatic hypotensive, and sedative effects of tricyclic antidepressants. The low incidence of anticholinergic effects associated with citalopram and other selective serotonin-reuptake inhibitors compared with tricyclic antidepressants is a potential advantage in geriatric patients, since such effects (e.g., constipation, dry mouth, confusion, memory impairment) may be particularly troublesome in these patients. Some clinicians state that selective serotonin-reuptake inhibitors including citalopram may be preferred for treating depression in geriatric patients in whom the orthostatic hypotension associated with many antidepressants (e.g., tricyclics) potentially may result in injuries (such as severe falls). However, despite the fewer cardiovascular and anticholinergic effects associated with selective serotonin-reuptake inhibitors, these drugs did not show any advantage over tricyclic antidepressants with regard to hip fracture in a case-control study. In addition, there was little difference in the rates of falls between nursing home residents receiving selective serotonin-reuptake inhibitors and those receiving tricyclic antidepressants in a retrospective study. Therefore, all geriatric patients receiving either type of antidepressant should be considered at increased risk of falls and appropriate measures should be taken.

Patients with dementia of the Alzheimer's type (Alzheimer's disease, presenile or senile dementia) often present with depressive symptoms, such as depressed mood, appetite loss, insomnia, fatigue, irritability, and agitation. Most experts recommend that patients with dementia of the Alzheimer's type and depressive symptoms be considered as candidates for pharmacotherapy even if they fail to meet the criteria for a major depressive syndrome. The goals of such therapy are to improve mood, functional status (e.g., cognition), and quality of life. Although patients may present with depressed mood alone, the possibility of more extensive depressive symptomatology should be considered. Therefore, patients should be monitored carefully for indices of major depression, suicidal ideation, and neurovegetative signs since safety measures (e.g., hospitalization for suicidal ideations) and more vigorous and aggressive therapy (e.g., relatively high dosages, multiple drug trials) may be needed in some patients.

If pharmacotherapy is initiated for depressive symptoms in Alzheimer's patients, most experts recommend selective serotonin-reuptake inhibitors such as citalopram, escitalopram, fluoxetine, paroxetine, or sertraline as first-line therapy because of their favorable adverse effect profile in this population compared with other currently available antidepressants (e.g., tricyclic antidepressants, MAO inhibitors). Although evidence of efficacy from controlled studies currently is limited, the available evidence and experience with the use of antidepressants in patients with dementia of the Alzheimer's type and associated depressive manifestations indicate that depressive symptoms (including depressive mood alone and with neurovegetative changes) in such patients are responsive to antidepressant therapy. In some patients, cognitive deficits may partially or fully resolve during antidepressant therapy, but the extent of response will be limited to the degree of cognitive impairment that is directly related to depression. In a controlled study comparing citalopram and placebo in elderly patients with dementia, citalopram was found to improve depression as well as cognitive and emotional functioning more than placebo. In an open study in a limited number of patients with dementia and behavioral disturbances, citalopram was found to improve the behavioral complications associated with dementia†.

Cardiovascular Considerations. The relatively low incidence of adverse cardiovascular effects, including orthostatic hypotension and conduction disturbances, associated with citalopram and other selective serotonin-reuptake inhibitors may be advantageous in patients in whom the cardiovascular effects associated with tricyclic antidepressants may be hazardous. However, clinical studies of citalopram for the management of depression generally did not include individuals with cardiovascular disease (e.g., those with a recent history of myocardial infarction or unstable cardiovascular disease), and further experience in such patients is necessary to confirm the relative lack of cardiotoxicity reported with the drug to date. (See Cautions: Cardiovascular Effects and see Cautions: Precautions and Contraindications.)

Sedative Considerations. Because citalopram and other selective serotonin-reuptake inhibitors generally are less sedating than some other antidepressants (e.g., tricyclics), some clinicians state that these drugs may be preferable in patients who do not require the sedative effects associated with many antidepressant agents or in patients who are prone to accidents; however, an antidepressant with more prominent sedative effects may be preferable in certain patients (e.g., those with insomnia).

Suicidal Risk Considerations. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. However, there has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidal thinking and behavior (suicidality) in certain patients during the early phases of treatment. FDA states that antidepressants increased the risk of suicidality in short-term studies in children, adolescents, and young adults (18–24 years of age) with major depressive disorder and other psychiatric disorders. (See Cautions: Pediatric Precautions.) An increased suicidality risk was not demonstrated with antidepressants compared with placebo in adults older than 24 years of age and a reduced risk was observed in adults 65 years of age or older. It currently is unknown whether the suicidality risk extends to longer-term antidepressant use (i.e., beyond several months); however, there is substantial evidence from placebo-controlled maintenance trials in adults with major depressive disorder that antidepressants can delay the recurrence of depression. Because the risk of suicidality in depressed patients may persist until substantial remission of depression occurs, appropriate monitoring and close observation of patients of all ages who are receiving antidepressant therapy are recommended. (See Cautions: Precautions and Contraindications.)

Other Considerations. Citalopram has been effective in patients with moderate to severe depression, endogenous depression, post-stroke depression and pathologic crying, and depression associated with chronic hepatitis C virus infection.

In an open study in a limited number of patients with bipolar depression† (mainly bipolar I disorder), citalopram was effective and well tolerated when added to monotherapy or combined therapy with lithium, divalproex sodium, and/or carbamazepine. Controlled studies are needed to confirm these preliminary findings. The manufacturer states that citalopram is *not* approved for use in treating bipolar depression, and that the possibility that the drug may precipitate hypomanic or manic attacks in patients with bipolar or other major affective disorder should be considered. For detailed information on bipolar disorder, including its management, see Uses: Bipolar Disorder, in Lithium Salts 28:28.

In patients with refractory depression, citalopram was more effective when given in combination with buspirone in one placebo-controlled study. However, combined citalopram and buspirone therapy was not found to be more effective than citalopram monotherapy in another placebo-controlled study. In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) level 2 trial, patients with major depressive disorder who did not respond to or could not tolerate citalopram therapy were randomized to receive either extended-release ("sustained-release") bupropion or buspirone therapy in addition to citalopram. Although both extended-release bupropion and buspirone were found to produce similar remission rates, extended-release bupropion produced a greater reduction in the number and severity of symptoms and a lower rate of drug discontinuance than buspirone in this large-scale, effectiveness trial. These results suggest that augmentation of SSRI therapy with extended-release bupropion may be useful in some patients with refractory depression. The addition of lithium to citalopram in depressed patients not responding to citalopram alone also has been found to be effective and well tolerated in a double-blind, placebo-controlled trial. (See Drug Interactions: Lithium.)

In a limited number of depressed patients not responding to citalopram