**PSYCHOTROPIC DRUGS. PHARMACOLOGY OF PSYCHOLEPTICS (NEUROLEPTICS, TRANQUILIZERS, SEDATIVES AND LITHIUM SALTS)**

**ANTIPSYCHOTIC DRUGS**

The antipsychotic drugs are usually divided into first- and second generation agents. The first-generation drugs are further classified as "low potency" or "high potency." This classification does not indicate clinical effectiveness of the drugs but rather specifies affinity for the dopamine D2 receptor, which, in turn, may influence the adverse effect profile of the drug.

**1. Derivates of Phenothiazine**

Promazine, Chlorpromazine, Tizercine, Tioridazine, Pipotiazine, Pipotiazine-depo, Meterazine, Triphthazine, Ethaperazine, Fluphenazine, Fluphenazine-depo, Phrenolone

**2. Thioxanthines**

Chlorprotixene, Flupentixole, Flupentixole-depo

**3. Derivates of Butyrophenone**

Haloperidol, Droperidol

**4. Derivates of Diphenylbutylpiperidine**

Pimozid, Fluspirilene, Penfluridone

**5. Alkaloid of Rauwolfia plant**

Rezerpine

**6. Tricyclic Antipsychotics**

Clozapine, Olanzepine, Quetiapine

**7. Derivates of Benzyzoxazole**

Rispolepte

**8. Derivates of Benzamides**

Sulpiride, Sultopride, Tiapride

**9. Derivates of Indole and Carboline**

Carbidine

**A. First-generation antipsychotics.** The first-generation antipsychotic drugs (also called conventional) are competitive inhibitors at a variety of receptors, but their antipsychotic effects reflect competitive blockade of dopamine 0 2 receptors. First-generation antipsychotics are more likely to be associated with movement disorders known as extrapyramidal symptoms (EPS), particularly drugs that bind tightly to dopaminergic neuroreceptors, such as haloperidol. Movement disorders are somewhat less likely with medications that bind less potently, such as chlorpromazine. No one drug is clinically more effective than another.

**B. Second-generation antipsychotic drugs.** The second-generation antipsychotic drugs (also called "atypical" antipsychotics) have a lower incidence of EPS than the first-generation agents but are associated with a higher risk of metabolic adverse effects, such as diabetes, hypercholesterolemia, and weight gain. The second-generation drugs owe their unique activity to blockade of both serotonin and dopamine receptors.

**1. Drug selection:** Second-generation agents are generally used as first-line therapy for schizophrenia to minimize the risk of debilitating EPS associated with the first-generation drugs that act primarily at the dopamine D2 receptor. The second-generation antipsychotics exhibit an efficacy that is equivalent to, and occasionally exceeds, that of the first-generation antipsychotic agents. Differences in therapeutic efficacy among the second-generation drugs have not been established and individual patient response and comorbid conditions must often be used to guide drug selection.

**2. Refractory patients:** Approximately 10% to 20% of patients with schizophrenia have an insufficient response to first- and second-generation antipsychotics. For these patients, clozapine has shown to be an effective antipsychotic with a minimal risk of EPS. However, its clinical use is limited to refractory patients because of serious adverse effects. Clozapine can produce bone marrow suppression, seizures, and cardiovascular side effects, such as orthostatic. The risk of severe agranulocytosis necessitates frequent monitoring of white blood cell counts.

**C. Mechanism of action**

1. Dopamine antagonism: All of the first-generation and most of the second-generation antipsychotic drugs block D2 dopamine receptors in the brain and the periphery.

2. Serotonin receptor-blocking activity: Most of the second-generation agents exert part of their action through inhibition of serotonin receptors (5-HT), particularly 5-HT2A receptors. Clozapine has high affinity for D1, D4, 5-HT2, muscarinic, and a-adrenergic receptors, but it is also a weak dopamine D2 receptor antagonist. Risperidone blocks 5-HT2A receptors largely than it does D2 receptors, as doe’s olanzapine. The second-generation antipsychotics aripiprazole, brexpiprazole, and cariprazine are partial agonists at D2 and 5-HT1A receptors, as well as antagonists of 5-HT2A receptors. Quetiapine is relatively weak at blockade of D2 and 5-HT2A receptors. Its low risk for EPS may also be related to the relatively short period of time it binds to the D2 receptor. Pimavanserin appears to act as an inverse agonist and antagonist at the 5-HT2A receptor and the 5-HT2c receptor, with no appreciable affinity for dopamine receptors. Pimavanserin is indicated for psychosis associated with Parkinson disease.

**D. Actions**

The clinical effects of antipsychotic drugs reflect a blockade at dopamine and/or serotonin receptors. However, many antipsychotic agents also block cholinergic, adrenergic, and histaminergic receptors. It is unknown what role, if any, these actions have in alleviating the symptoms of psychosis. However, the undesirable adverse effects of antipsychotic drugs often result from pharmacological actions at these other receptors.

**1. Antipsychotic effects:** All antipsychotic drugs can reduce hallucinations and delusions associated with schizophrenia {known as "positive" symptoms) by blocking D2 receptors in the mesolimbic system of the brain. The "negative" symptoms, such as blunted affect, apathy, and impaired attention, as well as cognitive impairment, are not as responsive to therapy, particularly with the first generation antipsychotics. Many second-generation agents, such as clozapine, can ameliorate the negative symptoms to some extent.

**2. Extrapyramidal effects:** Dystonia’s {sustained contraction of muscles leading to twisting, distorted postures), Parkinson-like symptoms, akathisia {motor restlessness), and tardive dyskinesia {involuntary movements, usually of the tongue, lips, neck, trunk, and limbs) can occur with both acute and chronic treatment. Blockade of dopamine receptors in the nigrostriatal pathway is believed to cause these unwanted movement symptoms. The second-generation antipsychotics exhibit a lower incidence of EPS.

**3. Antiemetic effects:** The antipsychotic drugs have antiemetic effects that are mediated by blocking D2 receptors of the chemoreceptor trigger zone of the medulla.

**4. Anticholinergic effects**: Some of the antipsychotics, particularly thioridazine, chlorpromazine, clozapine, and olanzapine, produce anticholinergic effects. These effects include blurred vision, dry mouth (the exception is clozapine, which increases salivation), confusion, and inhibition of gastrointestinal and urinary tract smooth muscle, leading to constipation and urinary retention. The anticholinergic effects may actually assist in reducing the risk of EPS with these agents.

**5. Other effects:** Blockade of a-adrenergic receptors causes orthostatic hypotension and light-headedness. The antipsychotics also alter temperature-regulating mechanisms and can produce poikilothermia (condition in which body temperature varies with the environment). In the pituitary, antipsychotics that block D2 receptors may cause an increase in prolactin release. Sedation occurs with those drugs that are potent antagonists of the H1-histamine receptor, including chlorpromazine, olanzapine, quetiapine, and clozapine. Sexual dysfunction may also occur with the antipsychotics due to various receptor-binding characteristics. Weight gain is also a common adverse effect of antipsychotics and is more significant with the secondgeneration agents.

**E. Therapeutic uses**

**1. Treatment of schizophrenia:** The antipsychotics are the only efficacious pharmacological treatment for schizophrenia. The first generation antipsychotics are generally most effective in treating the positive symptoms of schizophrenia. The atypical antipsychotics with 5-HT2A receptor-blocking activity may be effective in many patients who are resistant to the traditional agents, especially in treating the negative symptoms of schizophrenia.

**2. Prevention of nausea and vomiting:** The older antipsychotics (most commonly, prochlorperazine) are useful in the treatment of drug-induced nausea.

**3. Other uses:** The antipsychotic drugs can be used as tranquilizers to manage agitated and disruptive behavior secondary to other disorders. Chlorpromazine is used to treat intractable hiccups. Pimozide is primarily indicated for treatment of the motor and phonic tics of Tourette disorder. However, risperidone and haloperidol are also commonly prescribed for this tic disorder. Also, risperidone and aripiprazole are approved for the management of disruptive behavior and irritability secondary to autism. Many antipsychotic agents are approved for the management of the manic and mixed symptoms associated with bipolar disorder. Lurasidone and quetiapine are indicated for the treatment of bipolar depression. Paliperidone is approved for the treatment of schizoaffective disorder. Some antipsychotics (aripiprazole, brexpiprazole, and quetiapine) are used as adjunctive agents with antidepressants for treatment-refractory depression.

**F. Absorption and metabolism**

After oral administration, the antipsychotics show variable absorption that is unaffected by food (except for ziprasidone, lurasidone, and paliperidone, the absorption of which is increased with food). These agents readily pass into the brain and have a large volume of distribution. They are metabolized to many different metabolites, usually by the cytochrome P-450 system in the liver, particularly the CYP2D6, CYP1A2, and CYP3A4 isoenzymes. Some metabolites are active and have been developed as pharmacological agents themselves (for example, paliperidone is the active metabolite of risperidone, and the antidepressant amoxapine is the active metabolite of loxapine). Fluphenazine decanoate, haloperidol decanoate, risperidone microspheres, paliperidone palmitate, aripiprazole monohydrate, aripiprazole lauroxil, and olanzapine pamoate are long-acting injectable (LAI) formulations of antipsychotics. These formulations usually have a therapeutic duration of action of 2 to 4 weeks, with some having a duration of 6 to 12 weeks. Therefore, these LAI formulations are often used to treat outpatients and individuals who are nonadherent with oral medications.

**G. Adverse effects**

Adverse effects of the antipsychotic drugs can occur in practically all patients and are significant in about 80%.

**1. Extrapyramidal effects:** The inhibitory effects of dopaminergic neurons are normally balanced by the excitatory actions of cholinergic neurons in the striatum. Blocking dopamine receptors alters this balance, causing a relative excess of cholinergic influence, which results in extrapyramidal motor effects. The appearance of the movement disorders is generally time- and dose dependent, with dystonias occurring within a few hours to days of treatment, followed by akathisias occurring within days to weeks. Parkinson-like symptoms of bradykinesia, rigidity, and tremor usually occur within weeks to months of initiating treatment. Tardive dyskinesia (see below), which can be irreversible, may occur after months or years of treatment. If cholinergic activity is also blocked, a new, more nearly normal balance is restored, and extrapyramidal effects are minimized. This can be achieved by administration of an anticholinergic drug, such as benztropine. The therapeutic trade-off is a lower incidence of EPS in exchange for the adverse effect of muscarinic receptor blockade. Akathisia may respond better to β-blockers (for example, propranolol or benzodiazepines, rather than anticholinergic medications.

**2. Tardive dyskinesia:** Long-term treatment with antipsychotics can cause this motor disorder. Patients display involuntary movements, including bilateral and facial jaw movements and "fly-catching" motions of the tongue. A prolonged holiday from antipsychotics may cause the symptoms to diminish or disappear within a few months. However, in many individuals, tardive dyskinesia isirreversible and persists after discontinuation of therapy. Tardive dyskinesia is postulated to result from an increased number of dopamine receptors that are synthesized as a compensatory response to long-term dopamine receptor blockade. This makes the neuron supersensitive to the actions of dopamine, and it allows the dopaminergic input to this structure to overpower the cholinergic input, causing excess movement in the patient. Traditional antiEPS medications may actually worsen this condition. Valbenazine and deutetrabenazine are inhibitors of the vesicular monoamine transporter, and they are indicated for the management of tardive dyskinesia. These agents cause a decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores, ideally focused on dopamine, to address the symptoms of tardive dyskinesia.

**3. Neuroleptic malignant syndrome:** This potentially fatal reaction to antipsychotic drugs is characterized by muscle rigidity, fever, altered mental status and stupor, unstable blood pressure, and myoglobinemia. Treatment necessitates discontinuation of the antipsychotic agent and supportive therapy. Administration of dantrolene or bromocriptine may be helpful.

**4. Other effects:** Drowsiness occurs during the first few weeks of treatment. These agents may also cause confusion. Those antipsychotics with potent anti muscarinic activity often produce dry mouth, urinary retention, constipation, and loss of visual accommodation. Others may block a-adrenergic receptors, resulting in lowered blood pressure and orthostatic hypotension. The antipsychotics depress the hypothalamus, thereby affecting thermoregulation and causing amenorrhea, galactorrhea, gynecomastia, infertility, and erectile dysfunction. Significant weight gain is often a reason for nonadherence. Glucose and lipid profiles should be monitored in patients taking antipsychotics, as the second-generation agents may increase these laboratory parameters and possibly exacerbate preexisting diabetes or hyperlipidemia. Some antipsychotics have been associated with mild to significant QT prolongation. Thioridazine has the highest risk, and ziprasidone have cautions with their use due to this effect. Other antipsychotics have a general precaution regarding QT prolongation, even if the risk is relatively low.

**5. Cautions and contraindications:** All antipsychotics may lower the seizure threshold and should be used cautiously in patients with seizure disorders or those with an increased risk for seizures, such as withdrawal from alcohol. These agents also carry the warning of increased risk for mortality when used in elderly patients with dementia-related behavioral disturbances and psychosis. Antipsychotics used in patients with mood disorders should also be monitored for worsening of mood and suicidal ideation or behaviors.

**H. Maintenance treatment**

Patients who have had two or more psychotic episodes secondary to schizophrenia should receive maintenance therapy for at least 5 years, and some experts prefer indefinite therapy. The rate of relapse may be lower with second-generation drugs.

**ANXIOLYTIC DRUGS**

**Derivates of Benzodiazepine**

Chlozepide, Sibazone, Phenazepame, Nozepame, Lorazepame, Mezapame, Gidazepame, Clobazame, Alprazolame, Tetrazepame

**Derivates of Benzodiazepine**

Chlozepide, Sibazone, Phenazepame, Nozepame, Lorazepame, Mezapame, Gidazepame, Clobazame, Alprazolame, Tetrazepame

**Derivates of propandiole**

Meprotane

**Derivates of Diphenylmethane**

Amizyle

**Drugs from different groups**

Oxilidine, Mebicare, Trioxazine, Grandaxine

BENZODIAZEPINES

Benzodiazepines are widely used anxiolytic drugs. They have largely replaced barbiturates and meprobamate in the treatment of anxiety and insomnia, because benzodiazepines are generally considered to be safer and more effective. Though benzodiazepines are commonly used, they are not necessarily the best choice for anxiety or insomnia. Certain antidepressants with anxiolytic action, such as the selective serotonin reuptake inhibitors (SSRis), are preferred in many cases, and nonbenzodiazepine hypnotics and antihistamines may be preferable for insomnia.

**A. Mechanism of action**

The targets for benzodiazepine actions are the γ-aminobutyric acid GABAA receptors. The GABAA receptors are composed of a combination of five a-, β- and γ-subunits that span the postsynaptic membrane. For each subunit, many subtypes exist (for example, there are six subtypes of the α-subunit). Binding of GABA to its receptor triggers an opening of the central ion channel, allowing chloride through the pore. The influx of chloride ions causes hyperpolarization of the neuron and decreases neurotransmission by inhibiting the formation of action potentials. Benzodiazepines modulate GABA effects by binding to a specific, high-affinity site (distinct from the GABA-binding site) located at the interface of the α-subunit and the y subunit on the GABAA receptor. Benzodiazepines increase the frequency of channel openings produced by GABA. The clinical effects of individual benzodiazepines correlate well with the binding affinity of each drug for the GABA receptor-chloride ion channel complex.

**B. Actions**

All benzodiazepines exhibit the following actions to some extent:

**1. Reduction of anxiety:** At low doses, the benzodiazepines are anxiolytic. They are thought to reduce anxiety by selectively enhancing GABA-ergic transmission in neurons having the α2-subunit in their GABAA receptors, thereby inhibiting neuronal circuits in the limbic system of the brain.

**2. Sedative/hypnotic:** All benzodiazepines have sedative and calming properties, and some can produce hypnosis (artificially produced sleep) at higher doses. The hypnotic effects are mediated by the a1-GABAA receptors.

**3. Anterograde amnesia:** Temporary impairment of memory with the use of the benzodiazepines is also mediated by the α1-GABAA receptors. The ability to learn and form new memories is also impaired.

**4. Anticonvulsant:** This effect is partially, although not completely, mediated by a 1-GABAp, receptors.

**5. Muscle relaxant:** At high doses, the benzodiazepines relax the spasticity of skeletal muscle, probably by increasing presynaptic inhibition in the spinal cord, where the α2-GABAA receptors are largely located.

**C. Therapeutic uses**

The individual benzodiazepines show small differences in their relative anxiolytic, anticonvulsant, and sedative properties. However, pharmacokinetic considerations are often important in choosing one benzodiazepine over another.

**1. Anxiety disorders:** Benzodiazepines are effective for the treatment of anxiety associated with panic disorder, generalized anxiety disorder (GAD), social anxiety disorder, performance anxiety, and extreme phobias, such as fear of flying. The benzodiazepines are also useful in treating anxiety related to depression and schizophrenia. These drugs should be reserved for severe anxiety and should not be used to manage the stress of everyday life. Because of their addictive potential, they should only be used for short periods of time. The longer-acting agents, such as clonazepam, lorazepam, and diazepam, are often preferred in patients with anxiety that require prolonged treatment. The antianxiety effects of the benzodiazepines are less subject to tolerance than the sedative and hypnotic effects. For panic disorders, alprazolam is effective for short- and long-term treatment, although it may cause withdrawal reactions in approximately 30% of patients.

**2. Sleep disorders:** Benzodiazepine hypnotics decrease the latency to sleep onset and increase stage II of non-rapid eye movement (REM) sleep. Both REM sleep and slow-wave sleep are decreased. In the treatment of insomnia, it is important to balance the sedative effect needed at bedtime with the residual sedation ("hangover'') upon awakening. Short-acting triazolam is effective in treating individuals who have problems falling asleep. The risk of withdrawal and rebound insomnia is higher with triazolam than with other agents. Intermediate-acting temazepam is useful for patients who experience frequent awakenings and have difficulty staying asleep. Temazepam should be administered 1 to 2 hours before the desired bedtime. Long-acting flurazepam is rarely used, due to its extended half-life, which may result in excessive daytime sedation and accumulation of the drug, especially in the elderly. Estazolam and quazepam are considered intermediate- and long-acting agents, respectively. In general, hypnotics should be used for only a limited time, usually 1 to 3 weeks.

**3. Amnesia:** The shorter-acting agents are often employed as premedication for anxiety-provoking and unpleasant procedures, such as endoscopy, dental procedures, and angioplasty. They cause a form of conscious sedation, allowing the patient to be receptive to instructions during these procedures. Midazolam is a benzodiazepine used to facilitate anterograde amnesia while providing sedation prior to anesthesia.

**4. Seizures:** Clonazepam is occasionally used as an adjunctive therapy types of seizures, whereas lorazepam and diazepam are the drugs of choice in terminating status epilepticus. Due to cross-tolerance, chlordiazepoxide, clorazepate, diazepam, lorazepam, and oxazepam are useful in the acute treatment of alcohol withdrawal and reduce the risk of withdrawal-related seizures.

**5. Muscular disorders:** Diazepam is useful in the treatment of skeletal muscle spasms and in treating spasticity from degenerative disorders, such as multiple sclerosis and cerebral palsy.

**D. Pharmacokinetics**

**1. Absorption and distribution:** The benzodiazepines are lipophilic. They are rapidly and completely absorbed after oral administration, distribute throughout the body, and penetrate into the CNS.

**2. Duration of action:** The half-lives of the benzodiazepines are important clinically, because the duration of action may determine the therapeutic usefulness. The benzodiazepines can be roughly divided into short-, intermediate-, and long-acting groups. The longer-acting agents form active metabolites with long half-lives. However, with some benzodiazepines, the clinical duration of action does not correlate with the actual halflife (otherwise, a dose of diazepam could conceivably be given only every other day, given its long half-life and active metabolites). This may be due to receptor dissociation rates in the CNS and subsequent redistribution to fatty tissues and other areas.

**3. Fate:** Most benz.odiazepines, including ch/ordiazepoxkie and diazepam, are metabolized by the hepatic microsomal system to compounds that are also active. For these benzodiazepines, the apparent half-life of the drug represents the combined actions of the parent drug and its metabolites. The benzodiazepines are excreted in the urine as glucuronides or oxidized metabolites. All benzodiazepines cross the placenta and may depress the CNS of the newborn if given before birth. The benzodiazepines are not recommended for use during pregnancy. Nursing infants may also be exposed to the drugs in breast milk.

**E. Dependence**

Psychological and physical dependence can develop if high doses of benzodiazepines are given for a prolonged period. All benzodiazepines are controlled substances. Abrupt discontinuation of these agents results in withdrawal symptoms, including confusion, anxiety, agitation, restlessness, insomnia, tension, and (rarely) seizures. Benzodiazepines with a short elimination half-life, such as triazolam, induce more abrupt and severe withdrawal reactions than those seen with drugs that are slowly eliminated such as flurazepam.

**F. Adverse effects**

Drowsiness and confusion are the most common adverse effects of the benzodiazepines. Ataxia occurs at high doses and precludes activities that require fine motor coordination, such as driving an automobile. Cognitive impairment (decreased recall and retention of new knowledge) can occur with use of benzodiazepines. Benzodiazepines should be used cautiously in patients with liver disease. Alcohol and other CNS depressants enhance the sedative-hypnotic effects of the benzodiazepines. Benzodiazepines are, however, considerably less dangerous than the older anxiolytic and hypnotic drugs. As a result, a drug overdose is seldom lethal unless other central depressants, such as alcohol or opioids, are taken concurrently.

**BENZODIAZEPINE ANTAGONIST**

Flumazenil is a GABA receptor antagonist that rapidly reverses the effects of benzodiazepines. The drug is available for intravenous (IV) administration only. Onset is rapid, but the duration is short, with a half-life of about 1 hour. Frequent administration may be necessary to maintain reversal of a long-acting benzodiazepine. Administration of flumazenil may precipitate withdrawal in dependent patients or cause seizures if a benzodiazepine is used to control seizure activity. Seizures may also result if the patient has a mixed ingestion with tricyclic antidepressants or antipsychotics. Dizziness, nausea, vomiting, and agitation are the most common adverse effects.

**OTHER ANXIOLYTIC AGENTS**

**A. Antidepressants**

Many antidepressants are effective in the treatment of chronic anxiety disorders and should be considered as first-line agents, especially in patients with concerns for addiction or dependence. SSRis (such as escitalopram or paroxetine) or serotonin/norepinephrine reuptake inhibitors (SNRis, such as venlafaxine or duloxetine) may be used alone or prescribed in combination with a benzodiazepine during the first week of treatment. After 4 to 6 weeks, when the antidepressant begins to produce an anxiolytic effect, the benzodiazepine dose can be tapered. While only certain SSRis or SNRis have been approved for the treatment of anxiety disorders such as GAD, the efficacy of these drugs is most likely a class effect. Long-term use of antidepressants and benzodiazepines for anxiety disorders is often required to maintain ongoing benefit and prevent relapse.

**B. Buspirone**

Buspirone is useful for the chronic treatment of GAD and has an efficacy comparable to that of benzodiazepines. It has a slow onset of action and is not effective for short-term or "as-needed" treatment of acute anxiety. The actions of buspirone appear to be mediated by serotonin (5-HT1A) receptors, although it also displays some affinity for D2 dopamine receptors and 5-HT2A serotonin receptors. Thus, its mode of action differs from that of the benzodiazepines. In addition, buspirone lacks the anticonvulsant and muscle-relaxant properties of the benzodiazepines. The frequency of adverse effects is low, with the most common effects being headache, dizziness, nervousness, nausea, and light-headedness. Sedation and psychomotor and cognitive dysfunction are minimal, and dependence is unlikely. Buspirone does not potentiate the CNS depression of alcohol.

**SEDATIVE DRUGS**

**Bromides**

Sodium bromide, Potassium bromide, Bromcamphora

**Motherwort (Leonurum) Drugs**

Tincture of Leonurum, Fluid extract of Leonurum

**Passion-flower Drugs**

Fluid extract of Passion-flower, Passit

**Valerian Drugs**

Infusion of roots of Valerian, Drops of Camphor with Valerian, Valocormide, Valosedane, Corvalole, Valocordine

**LITHIUM SALTS**

Lithium carbonate (Escalith), Lithium oxibutirate, Micalite, Lithionite, Lithionite-durel, Lithium-durulez, Quilone-retard, Contemnole-retard

Lithium salts are used acutely and prophylactically for managing bipolar patients. Lithium is effective in treating 60% to 80% of patients exhibiting mania and hypomania. Although many cellular processes are altered by treatment with lithium, the mode of action is unknown. The therapeutic index of lithium is extremely low, and lithium can be toxic. Common adverse effects may include headache, dry mouth, polydipsia, polyuria, polyphagia, Gl distress, fine hand tremor, dizziness, fatigue, dermatologic reactions, and sedation. Adverse effects due to higher plasma levels may indicate toxicity and include ataxia, slurred speech, coarse tremors, confusion, and convulsions. Thyroid function may be decreased and should be monitored. Lithium is renally eliminated, and though caution should be used when dosing this drug in renally impaired patients, it may be the best choice in patients with hepatic impairment.