For the use of a psychiatrist or a Hospital or a Laboratory only

ILOBRIL
(ILOPERIDONE TABLETS)

COMPOSITION

ILOBRIL 1
Iloperidone Tablets 1 mg
Each uncoated tablet contains:
Iloperidone I.P. 1 mg

ILOBRIL 2
Iloperidone Tablets 2 mg
Each uncoated tablet contains:
Iloperidone I.P. 2 mg

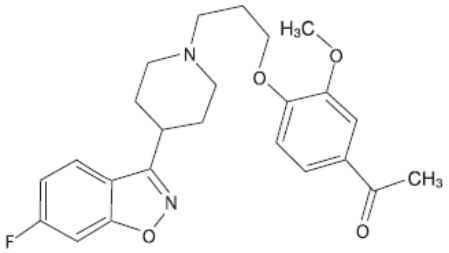
ILOBRIL 4
Iloperidone Tablets 4 mg
Each uncoated tablet contains:
Iloperidone I.P. 4 mg

ILOBRIL 6
Iloperidone Tablets 6 mg
Each uncoated tablet contains:
Iloperidone I.P. 6 mg

ILOBRIL 8
Iloperidone Tablets 8 mg
Each uncoated tablet contains:
Iloperidone I.P. 8 mg

DESCRIPTION:

Iloperidone is a psychotropic agent belonging to the chemical class of piperidinyl-benzisoxazole derivatives. Its chemical name is 4'-[3-[4-(6-Fluoro-1, 2-benzisoxazol-3-yl) piperidino] propoxy] -3'-methoxy acetophenone. Its molecular formula is $C_{24}H_{27}FN_2O_4$ and its molecular weight is 426.48. The structural formula is:



CLINICAL PHARMACOLOGY

Mechanism of Action

The mechanism of action of Iloperidone, as with other drugs having efficacy in schizophrenia, is unknown. However it is proposed that the efficacy of Iloperidone is mediated through a combination of dopamine type 2 (D_2) and serotonin type 2 ($5\text{-}HT_2$) antagonisms.

Pharmacodynamics

Iloperidone exhibits high affinity binding to serotonin $5\text{-}HT_{2A}$ and dopamine D_2 and D_3 receptors. Iloperidone has moderate affinity for dopamine D_4, serotonin $5\text{-}HT_6$ and $5\text{-}HT_7$, and norepinephrine $NE\alpha_1$ receptors and low affinity for the serotonin $5\text{-}HT_{1A}$, dopamine D_1 and histamine H_1 receptors. Iloperidone has no appreciable affinity for cholinergic muscarinic receptors. Iloperidone functions as an antagonist at the dopamine D_2, D_3, serotonin $5\text{-}HT_{1A}$ and norepinephrine α_1/α_2C receptors. The affinity of the Iloperidone metabolite P88 is generally equal or less than that of the parent compound. In contrast, the metabolite P95 only shows affinity for $5\text{-}HT_{2A}$ and the $NE\alpha_{1A}$, $NE\alpha_{1B}$, $NE\alpha_{1D}$, and $NE\alpha_{2C}$ receptors.

Pharmacokinetics

Iloperidone is well absorbed after administration of the tablet with peak plasma concentrations occurring within 2 to 4 hours. Iloperidone has an apparent clearance (clearance / bioavailability) of 47 to 102 L/h, with an apparent volume of distribution of 1340-2800 L. At therapeutic concentrations, iloperidone and its metabolites are ~ 95% bound to serum proteins. Iloperidone is metabolized primarily by three biotransformation pathways: carbonyl reduction, hydroxylation (mediated by CYP2D6) and O-demethylation (mediated by CYP3A4). There are two predominant iloperidone metabolites, P95 and P88. The iloperidone metabolite P95 represents 47.9% of the AUC of iloperidone and its metabolites in plasma at steady-state for extensive metabolizers (EM) and 25% for poor metabolizers (PM). The active metabolite P88 accounts for 19.5% and 34.0% of total plasma exposure in EM and PM, respectively. Approximately 7-10% of Caucasians and 3-8% of Black/African Americans lack the capacity to metabolize CYP2D6 substrates and are classified as poor metabolizers (PM), whereas the rest are intermediate, extensive or ultrarapid metabolizers. Co-administration of iloperidone with known strong inhibitors of CYP2D6 like fluoxetine results in a 2.3 fold increase in iloperidone plasma exposure, and therefore one-half of the iloperidone dose should be administered. Similarly, PMs of CYP2D6 have higher exposure to iloperidone compared with EMs and PMs should have their dose reduced by one-half. Laboratory tests are available to identify CYP2D6 PMs.

INDICATIONS AND USAGE

Iloperidone tablets are indicated for the acute treatment of adults with schizophrenia. When deciding among the alternative treatments available for this condition, the prescriber should consider the finding that iloperidone is associated with prolongation of the QTc interval. Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsade de pointes-type arrhythmia, a potentially fatal polymorphic ventricular tachycardia which can result in sudden death. In many cases this would lead to the conclusion that other drugs should be tried first. Whether iloperidone will cause torsade de pointes or increase the rate of sudden death is not yet known. Patients must be titrated to an effective dose of iloperidone. Thus, control of symptoms may be delayed during the first 1 to 2 weeks of treatment compared to some other antipsychotic drugs that do not require a similar titration. Prescribers should be mindful of this delay when selecting an antipsychotic drug for the acute treatment of schizophrenia.The

physician who elects to use iloperidone for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

DOSAGE AND ADMINISTRATION

Usual Dose

Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension due to its alpha-adrenergic blocking properties. The recommended starting dose for iloperidone tablets is 1 mg twice daily. Increases to reach the target dose range of 6-12 mg twice daily may be made with daily dosage adjustments to 2 mg twice daily, 4 mg twice daily and 6 mg twice daily, on days 2, 3 and 4 respectively. Efficacy was demonstrated with iloperidone in a dose range of 6 to 12 mg twice daily. Prescribers should be mindful of the fact that patients need to be titrated to an effective dose of iloperidone by increments of 2 mg twice daily up to maximum dose of 12 mg twice daily. Thus, control of symptoms may be delayed during the first 1 to 2 weeks of treatment compared to some other antipsychotic drugs that do not require similar titration. Prescribers should also be aware that some adverse effects associated with iloperidone use are dose related. The maximum recommended dose is 12 mg twice daily (24 mg/day); iloperidone doses above 24 mg/day have not been systematically evaluated in the clinical trials. Iloperidone can be administered without regard to meals.

Dosage in Special Populations

Dosage adjustments are not routinely indicated on the basis of age, gender, race, or renal impairment status.

Dosage adjustment for patients taking Iloperidone concomitantly with potential CYP2D6 inhibitors:

Iloperidone dose should be reduced by one-half when administered concomitantly with strong CYP2D6 inhibitors such as fluoxetine or paroxetine. When the CYP2D6 inhibitor is withdrawn from the combination therapy, iloperidone dose should then be increased to where it was before.

Dosage adjustment for patients taking Iloperidone concomitantly with potential CYP3A4 inhibitors:

Iloperidone dose should be reduced by one-half when administered concomitantly with strong CYP3A4 inhibitors such as ketoconazole or clarithromycin. When the CYP3A4 inhibitor is withdrawn from the combination therapy, iloperidone dose should be increased to where it was before.

Dosage adjustment for patients taking Iloperidone who are poor metabolizers of CYP2D6: Iloperidone dose should be reduced by one-half for poor metabolizers of CYP2D6.

Hepatic Impairment: Iloperidone is not recommended for patients with hepatic impairment

Maintenance Treatment

Although there is no body of evidence available to answer the question of how long the patient treated with iloperidone should be maintained, it is generally recommended that responding patients be continued beyond the acute response. Patients should be periodically reassessed to determine the need for maintenance treatment.

Reinitiation of Treatment in Patients Previously Discontinued
Although there are no data to specifically address re-initiation of treatment, it is recommended that the initiation titration schedule be followed whenever patients have had an interval off iloperidone of more than 3 days.

Switching from Other Antipsychotics
There are no specific data to address how patients with schizophrenia can be switched from other antipsychotics to iloperidone or how iloperidone can be used concomitantly with other antipsychotics. Although immediate discontinuation of the previous antipsychotic treatment may be acceptable for some patients with schizophrenia, more gradual discontinuation may be most appropriate for others. In all cases, the period of overlapping antipsychotic administration should be minimized.

USE IN SPECIFIC POPULATIONS
Pregnancy
Iloperidone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery
The effect of iloperidone on labor and delivery in humans is unknown.

Nursing Mothers
It is recommended that women receiving iloperidone should not breast feed.

Pediatric Use
Safety and effectiveness in pediatric and adolescent patients have not been established.

Geriatric Use
Clinical Studies of iloperidone in the treatment of schizophrenia did not include sufficient numbers of patients aged 65 years and over to determine whether or not they respond differently than younger adult patients. Studies of elderly patients with psychosis associated with Alzheimer's disease have suggested that there may be a different tolerability profile (i.e., increased risk in mortality and cerebrovascular events including stroke) in this population compared to younger patients with schizophrenia. The safety and efficacy of iloperidone in the treatment of patients with psychosis associated with Alzheimer's disease has not been established. If the prescriber elects to treat such patients with iloperidone, vigilance should be exercised.

Renal Impairment
Because iloperidone is highly metabolized, with less than 1% of the drug excreted unchanged, renal impairment alone is unlikely to have a significant impact on the pharmacokinetics of iloperidone.

Hepatic Impairment
No dose adjustment to Iloperidone is needed in patients with mild hepatic impairment. Exercise caution when administering it to patients with moderate hepatic impairment. Iloperidone is not

recommended for patients with severe hepatic impairment. In adult subjects with mild hepatic impairment no relevant difference in pharmacokinetics of iloperidone, P88 or P95 (total or unbound) was observed compared to healthy adult controls. In subjects with moderate hepatic impairment a higher (2-fold) and more variable free exposure to the active metabolites P88 was observed compared to healthy controls, whereas exposure to iloperidone and P95 was generally similar (less than 50% change compared to control). Since a study in severe liver impaired subjects has not been conducted, Iloperidone is not recommended for patients with severe hepatic impairment.

Smoking Status
Iloperidone is not a substrate for CYP1A2; smoking should therefore not have an effect on the pharmacokinetics of iloperidone.

CONTRAINDICATIONS
Iloperidone is contraindicated in individuals with a known hypersensitivity reaction to the product.

Reactions have included pruritus and urticaria.

WARNINGS AND PRECAUTIONS

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA- RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analysis of seventeen placebo-controlled trials (modal duration 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature.

Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. This drug is not approved for the treatment of patients with Dementia-Related Psychosis

Increased Risks in Elderly Patients with Dementia-Related Psychosis
Iloperidone is not approved for the treatment of patients with dementia-related psychosis since it will increase risk of mortality and increase incidence of cerebrovascular adverse events (cerebrovascular accidents and transient ischemic attacks).

QT Prolongation
The use of iloperidone should be avoided in combination with other drugs that are known to prolong QTc including Class 1A (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, antipsychotic medications (e.g., chlorpromazine, thioridazine), antibiotics (e.g., gatifloxacin, moxifloxacin), or any other class of medications known to prolong the QTc interval (e.g., pentamidine, levomethadyl acetate, methadone). iloperidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. Certain circumstances may increase the risk of torsade de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval, including (1) bradycardia; (2) hypokalemia or hypomagnesemia; (3) concomitant use of other drugs that prolong the QTc interval; and (4) presence of congenital prolongation of the QT interval; (5) recent acute myocardial infarction; and/or (6) uncompensated heart failure.

Caution is warranted when prescribing iloperidone with drugs that inhibit iloperidone metabolism and in patients with reduced activity of CYP2D6. It is recommended that patients being considered for iloperidone treatment who are at risk for significant electrolyte disturbances have baseline serum potassium and magnesium measurements with periodic monitoring. Hypokalemia (and/or hypomagnesemia) may increase the risk of QT prolongation and arrhythmia. iloperidone should be avoided in patients with histories of significant cardiovascular illness, e.g., QT prolongation, recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmia. iloperidone should be discontinued in patients who are found to have persistent QTc measurements >500 ms.

If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias, e.g., dizziness, palpitations, or syncope, the prescriber should initiate further evaluation, including cardiac monitoring.

Neuroleptic Malignant Syndrome (NMS)
A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including Iloperidone.

Tardive Dyskinesia
Tardive dyskinesia is a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, which may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely on prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic administered increases. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic

treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, Iloperidone should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that (1) is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on iloperidone, drug discontinuation should be considered. However, some patients may require treatment with iloperidone despite the presence of the syndrome.

Hyperglycemia and Diabetes Mellitus
Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including iloperidone. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness.

Weight Gain
Weigth gain is reported in clinical trials. Report based on the pooled data from the four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies, the proportions of patients having a weight gain of $\geq$ 7% body weight was 12% for iloperidone 10-16 mg/day, 18% for iloperidone 20-24 mg/day, and 13% for iloperidone (combined doses) versus 4% for placebo. The mean weight change from baseline to endpoint in the short-term studies was -0.1 kg for placebo versus 2.0 kg for iloperidone -treated patients. Across all short- and long-term studies, the overall mean change from baseline at endpoint was 2.1 kg.

Seizures
As with other antipsychotics, iloperidone should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer's dementia. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older.

Orthostatic Hypotension and Syncope
Iloperidone can induce orthostatic hypotension associated with dizziness, tachycardia, and syncope. This reflects its $alpha_1$-adrenergic antagonist properties. Iloperidone should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction, ischemia, or conduction abnormalities), cerebrovascular disease, or conditions that predispose the patient to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension.

Leukopenia, Neutropenia and Agranulocytosis
Leukopenia, Neutropenia, and Agranulocytosis have been reported with antipsychotics. Possible risk factors for leukopenia/neutropenia include preexisting low white blood cell count (WBC) and history of drug induced leukopenia/neutropenia. Patients with a pre-existing low WBC or a history of drug induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and should discontinue iloperidone at the first sign of a decline in WBC in the absence of other causative factors. Patients with neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm^3) should discontinue iloperidone and have their WBC followed until recovery.

Hyperprolactinemia
As with other drugs that antagonize dopamine D_2 receptors, iloperidone elevates prolactin levels. Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadalsteroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds. Longstanding hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male patients.

Body Temperature Regulation
Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing iloperidone for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

Dysphagia
Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia. iloperidone and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Suicide
The possibility of a suicide attempt is inherent in psychotic illness, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for iloperidone should be written for the smallest quantity of tablets consistent with good patient management in order to reduce the risk of overdose.

Priapism
Drugs with alphaadrenergic blocking effects have been reported to induce priapism. Iloperidone shares this pharmacologic activity. Severe priapism may require surgical intervention.

Potential for Cognitive and Motor Impairment
Iloperidone, like other antipsychotics, has the potential to impair judgment, thinking or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that therapy with iloperidone does not affect them adversely.

DRUG INTERACTIONS
Given the primary CNS effects of iloperidone, caution should be used when it is taken in combination with other centrally acting drugs and alcohol. Due to its "1-adrenergic receptor antagonism, iloperidone has the potential to enhance the effect of certain antihypertensive agents.

Potential for Other Drugs to Affect Iloperidone
Iloperidone is not a substrate for CYP1A1, CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2E1 enzymes. This suggests that an interaction of iloperidone with inhibitors or inducers of these enzymes, or other factors, like smoking, is unlikely. Both CYP3A4 and CYP2D6 are responsible for iloperidone metabolism. Inhibitors of CYP3A4 (e.g., ketoconazole) or CYP2D6 (e.g., fluoxetine, paroxetine) can inhibit iloperidone elimination and cause increased blood levels.

Ketoconazole: Iloperidone doses should be reduced by about one-half when administered with ketoconazole or other inhibitors of CYP3A4 (e.g., itraconazole). When the CYP3A4 inhibitor is withdrawn from the combination therapy, the iloperidone dose should be returned to the previous level.

Fluoxetine: Iloperidone doses should be reduced by one-half when administered with fluoxetine. When fluoxetine is withdrawn from the combination therapy, the iloperidone dose should be returned to the previous level. Other strong inhibitors of CYP2D6 would be expected to have similar effects and would need appropriate dose reductions. When the CYP2D6 inhibitor is withdrawn from the combination therapy, iloperidone dose could then be increased to the previous level.

Paroxetine: When paroxetine is withdrawn from the combination therapy, the iloperidone dose should be returned to the previous level. Other strong inhibitors of CYP2D6 would be expected to have similar effects and would need appropriate dose reductions. When the CYP2D6 inhibitor is withdrawn from the combination therapy, iloperidone dose could then be increased to previous levels.

Paroxetine and Ketoconazole: Iloperidone with inhibitors of both of its metabolic pathways did not add to the effect of either inhibitor given alone. Iloperidone doses should therefore be reduced by about one-half if administered concomitantly with both a CYP2D6 and CYP3A4 inhibitor.

Potential for Iloperidone to affect Other Drugs
In vitro studies in human liver microsomes showed that iloperidone does not substantially inhibit the metabolism of drugs metabolized by the following cytochrome P450 isozymes: CYP1A1,

CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, or CYP2E1. Furthermore, in vitro studies in human liver microsomes showed that iloperidone does not have enzyme inducing properties, specifically for the following cytochrome P450 isozymes: CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP3A4 and CYP3A5.

Dextromethorphan: A study in healthy volunteers showed that changes in the pharmacokinetics of dextromethorphan (80 mg dose) when a 3 mg dose of iloperidone was co-administered resulted in a 17% increase in total exposure and a 26% increase in the maximum plasma concentrations (Cmax)of dextromethorphan. Thus, an interaction between iloperidone and other CYP2D6 substrates is unlikely.

Fluoxetine: A single 3 mg dose of iloperidone had no effect on the pharmacokinetics of fluoxetine (20 mg twice daily).

Midazolam (a sensitive CYP 3A4 substrate): A study in patients with schizophrenia showed a less than 50% increase in midazolam total exposure at iloperidone steady state (14 days of oral dosing at up to 10 mg iloperidone twice daily) and no effect on midazolam Cmax. Thus, an interaction between iloperidone and other CYP3A4 substrates is unlikely.

Drugs that Prolong the QT Interval
Iloperidone should not be used with any other drugs that prolong the QT interval.

ADVERSE REACTIONS

Reactions are categorized by MedDRA system organ class

Body as a Whole: Arthralgia, Fatigue, Musculoskeletal Stiffness, Weight Increased.

Blood and Lymphatic Disorders: Anemia, iron deficiency anemia; leucopenia

Cardiac Disorders: Palpitations, arrhythmia, atrioventricular block first degree, cardiac failure (including congestive and acute), tachycardia

Vascular Disorders: Orthostatic Hypotension, Hypotension

Ear and Labyrinth Disorders: Vertigo, tinnitus

Endocrine Disorders: Hypothyroidism

Eye Disorders: Conjunctivitis (including allergic), Vision Blurred, dry eye, blepharitis, eyelid edema, eye swelling, lenticular opacities, cataract, hyperemia (including conjunctival)

Gastrointestinal Disorders: Nausea, Dry Mouth, Diarrhea, Abdominal Discomfort , gastritis, salivary hypersecretion, fecal incontinence, mouth ulceration, aphthous stomatitis, duodenal ulcer, hiatus hernia, hyperchlorhydria, lip ulceration, reflux esophagitis, stomatitis

*General Disorders and Administrative Site Conditions:*Eedema (general, pitting, due to cardiac disease), difficulty in walking, thirst, hyperthermia

Hepatobiliary Disorders: Cholelithiasis

Investigations: Weight decreased, hemoglobin decreased, neutrophil count increased, hematocrit decreased

Metabolism and Nutrition Disorders: Increased appetite, dehydration, hypokalemia, fluid retention

Musculoskeletal and Connective Tissue Disorders: Myalgia, muscle spasms, torticollis

Nervous System Disorders: Dizziness, Somnolence, Extrapyramidal Disorder (Akathisia, Bradykinesia, Dyskinesia, Dystonia, Parkinsonism), Tremor, Lethargy, paraesthesia, psychomotor hyperactivity, restlessness, amnesia, nystagmus, restless legs syndrome

Psychiatric Disorders: Restlessness, aggression, delusion, hostility, libido decreased, paranoia, anorgasmia, confusional state, mania, catatonia, mood swings, panic attack, obsessive-compulsive disorder, bulimia nervosa, delirium, polydipsia psychogenic, impulse-control disorder, major depression

Renal and Urinary Disorders: Urinary incontinence, dysuria, pollakiuria, enuresis, nephrolithiasis, urinary retention, renal failure acute

Reproductive System and Breast Disorders: Erectile dysfunction, Ejaculation Failure, testicular pain, amenorrhea, breast pain, menstruation irregular, gynecomastia, menorrhagia, metrorrhagia, postmenopausal hemorrhage, prostatitis, Retrograde ejaculation

Respiratory, Thoracic and Mediastinal Disorders: Nasal Congestion, Dyspnea, epistaxis, asthma, rhinorrhea, sinus congestion, nasal dryness, dry throat, sleep apnea syndrome, dyspnea exertional

Skin disorder: Rash

Infections: Nasopharyngitis, Upper Respiratory Tract Infection

DRUG ABUSE AND DEPENDENCE

Patients should be evaluated carefully for a history of drug abuse, and such patients should be observed closely for signs of Iloperidone misuse or abuse (e.g. development of tolerance, increases in dose, drug-seeking behavior)

OVERDOSAGE
In general, reported signs and symptoms where those resulting from an exaggeration of the known pharmacological effects (e.g., drowsiness and sedation, tachycardia and hypotension) of iloperidone.

Management of Overdose
There is no specific antidote for iloperidone. Therefore appropriate supportive measures should be instituted. In case of acute overdose, the physician should establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. The possibility of obtundation, seizures or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous ECG monitoring to detect possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide and quinidine should not be used, as they have the potential for QT-prolonging effects that might be additive to those of iloperidone. Similarly, it is reasonable to expect that the alpha-blocking properties of bretylium might be additive to those of iloperidone, resulting in problematic hypotension. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids or sympathomimetic agents (epinephrine and dopamine should not be used, since beta stimulation may worsen hypotension in the setting of iloperidone-induced alpha blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered. Close medical supervision should continue until the patient recovers.

EXPIRY DATE:
Do not use later than expiry date.

STORAGE:
Store at a temperature not exceeding 30^{o}C, protected from light and moisture.
Keep out of reach of children

PRESENTATION
ILOBRIL 1, ILOBRIL 2, ILOBRIL 4 & ILOBRIL 6 mg tablets are available in blister strips pack of 2 tablets.

ILOBRIL 6 & ILOBRIL 8 mg tablets are also available in blister strips pack of 10 tablets.

MARKETED BY
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