Phentermine (Adipex)

Indications and Usage for Phentermine

Phentermine hydrochloride is indicated as a short-term (a few weeks) adjunct in a regimen of weight reduction based on exercise, behavioral modification and caloric restriction in the management of exogenous obesity for patients with an initial body mass index ≥ 30 kg/m^2, or ≥ 27 kg/m^2 in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia).

Phentermine Dosage and Administration

Exogenous Obesity

Dosage should be individualized to obtain an adequate response with the lowest effective dose.

The usual adult dose is one tablet (37.5 mg) daily, as prescribed by the physician, administered before breakfast or 1 to 2 hours after breakfast. The dosage may be adjusted to the patient’s need. For some patients, half tablet (18.75 mg) daily may be adequate, while in some cases it may be desirable to give half tablets (18.75 mg) two times a day.

Phentermine hydrochloride is not recommended for use in pediatric patients ≤ 16 years of age.

*Late evening medication should be avoided because of the possibility of resulting insomnia.*

Dosage Forms and Strengths

Tablets containing 37.5 mg Phentermine hydrochloride (equivalent to 30 mg Phentermine base).
Contraindications

- History of cardiovascular disease (e.g., coronary artery disease, stroke, arrhythmias, congestive heart failure, uncontrolled hypertension)
- During or within 14 days following the administration of monoamine oxidase inhibitors
- Hyperthyroidism
- Glaucoma
- Agitated states
- History of drug abuse
- Pregnancy [No candidate for our weight loss program]
- Nursing [No candidate for our weight loss program] Known hypersensitivity, or idiosyncrasy to the sympathomimetic amines

Warnings and Precautions

Co-administration With Other Drug Products for Weight Loss

Phentermine hydrochloride tablets are indicated only as short-term (a few weeks) monotherapy for the management of exogenous obesity. The safety and efficacy of combination therapy with Phentermine and any other drug products for weight loss including prescribed drugs, over-the-counter preparations, and herbal products, or serotonergic agents such as selective serotonin reuptake inhibitors (e.g., fluoxetine, sertraline, fluvoxamine, paroxetine), have not been established. Therefore, coadministration of Phentermine and these drug products is not recommended.

Primary Pulmonary Hypertension

Primary Pulmonary Hypertension (PPH) – a rare, frequently fatal disease of the lungs – has been reported to occur in patients receiving a combination of Phentermine with fenfluramine or dexfenfluramine. The possibility of an association between PPH and the use of Phentermine alone cannot be ruled out; there have been rare cases of PPH in patients who reportedly have taken Phentermine alone.

The initial symptom of PPH is usually dyspnea. Other initial symptoms include angina pectoris, syncope or lower extremity edema. Patients should be advised to report immediately any deterioration in exercise tolerance. Treatment should be discontinued in patients who develop new, unexplained symptoms of dyspnea, angina pectoris, syncope or lower extremity edema, and patients should be evaluated for the possible presence of pulmonary hypertension.

Valvular Heart Disease

Serious regurgitant cardiac valvular disease, primarily affecting the mitral, aortic and/or tricuspid valves, has been reported in otherwise healthy persons who had taken a combination of Phentermine with fenfluramine or dexfenfluramine for weight loss. The possible role of Phentermine in the etiology of these valvulopathies has not been established and their course in individuals after the drugs are stopped is not known. The possibility of an association between valvular heart disease and the use of Phentermine alone cannot be ruled out; there have been rare cases of valvular heart disease in patients who reportedly have taken Phentermine alone.
Development of Tolerance, Discontinuation in Case of Tolerance

When tolerance to the anorectant effect develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

Effect on the Ability to Engage in Potentially Hazardous Tasks

Phentermine may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Risk of Abuse and Dependence

Phentermine is related chemically and pharmacologically to amphetamine (d- and d/l-amphetamine) and other related stimulant drugs have been extensively abused. The possibility of abuse of Phentermine should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. See Drug Abuse and Dependence (9) and Overdosage (10). The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of over dosage.

Usage With Alcohol

Concomitant use of alcohol with Phentermine may result in an adverse drug reaction.

Use in Patients With Hypertension

Use caution in prescribing Phentermine for patients with even mild hypertension (risk of increase in blood pressure).

Use in Patients on Insulin or Oral Hypoglycemic Medications for Diabetes Mellitus

A reduction in insulin or oral hypoglycemic medications in patients with diabetes mellitus may be required.

Adverse Reactions

The following adverse reactions are described, or described in greater detail, in other sections:

- Primary pulmonary hypertension [see Warnings and Precautions (5.2)]
- Valvular heart disease [see Warnings and Precautions (5.3)]
- Effect on the ability to engage in potentially hazardous tasks [see Warnings and Precautions (5.5)]
- Withdrawal effects following prolonged high dosage administration [see Drug Abuse and Dependence (9.3)]
**The following adverse reactions to Phentermine have been identified:**

**Cardiovascular**
Primary pulmonary hypertension and/or regurgitant cardiac valvular disease, palpitation, tachycardia, elevation of blood pressure, ischemic events.

**Central Nervous System**
Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache, psychosis.

**Gastrointestinal**
Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances.

**Allergic**
Urticaria.

**Endocrine**
Impotence, changes in libido.

**Drug Interactions**

**Monoamine Oxidase Inhibitors**
Use of Phentermine is contraindicated during or within 14 days following the administration of monoamine oxidase inhibitors because of the risk of hypertensive crisis.

**Alcohol**
Concomitant use of alcohol with Phentermine may result in an adverse drug reaction.

**Insulin and Oral Hypoglycemic Medications**
Requirements may be altered [see *Warnings and Precautions (5.9)*].

**Adrenergic Neuron Blocking Drugs**
Phentermine may decrease the hypotensive effect of adrenergic neuron blocking drugs.
USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects

Pregnancy category X

Phentermine is contraindicated during pregnancy because weight loss offers no potential benefit to a pregnant woman and may result in fetal harm. A minimum weight gain, and no weight loss, is currently recommended for all pregnant women, including those who are already overweight or obese, due to obligatory weight gain that occurs in maternal tissues during pregnancy. Phentermine has pharmacologic activity similar to amphetamine (d- and d,l-amphetamine) [see Clinical Pharmacology (12.1)]. Animal reproduction studies have not been conducted with Phentermine. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

Nursing Mothers

It is not known if Phentermine is excreted in human milk; however, other amphetamines are present in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Geriatric Use

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Renal Impairment

Phentermine was not studied in patients with renal impairment. Based on the reported excretion of Phentermine in urine, exposure increases can be expected in patients with renal impairment. Use caution when administering Phentermine to patients with renal impairment [see Clinical Pharmacology (12.3)].
Drug Abuse and Dependence

Controlled Substance

Phentermine is a Schedule IV controlled substance.

Abuse

Phentermine is related chemically and pharmacologically to the amphetamines. Amphetamines and other stimulant drugs have been extensively abused and the possibility of abuse of Phentermine should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program.

Dependence

Abuse of amphetamines and related drugs may be associated with intense psychological dependence and severe social dysfunction. There are reports of patients who have increased the dosage of these drugs to many times than recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. A severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Over dosage

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of over dosage.

Acute Over dosage

Manifestations of acute over dosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, and panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include tachycardia, arrhythmia, hypertension or hypotension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea and abdominal cramps. Over dosage of pharmacologically similar compounds has resulted in fatal poisoning usually terminates in convulsions and coma.

Management of acute Phentermine hydrochloride intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard. Acidification of the urine increases Phentermine excretion. Intravenous phentolamine (Regitine®, CIBA) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates .

Chronic Intoxication

Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. See Drug Abuse and Dependence (9.3).