PRESCRIBING INFORMATION

IONAMIN®
(Phentermine as a Resin Complex)

15 mg and 30 mg Capsules

Anorexiant

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PRESCRIBING INFORMATION

IONAMIN Capsules
Phentermine as a Resin Complex Capsules

THERAPEUTIC CLASSIFICATION

Anorexiant

ACTIONS, CLINICAL PHARMACOLOGY

IONAMIN (phentermine resin complex) is a sympathomimetic amine with pharmacologic activity similar to the prototype drug of this class used in obesity, amphetamine (d- and dl-amphetamine). Actions include central nervous system stimulation and elevation of blood pressure. Tachyphylaxis and tolerance have been demonstrated with all drugs of this class in which these phenomena have been looked for.

Drugs of this class used in obesity are commonly known as "anorectics" or "anorexigenics". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects may be involved.

Adult obese subjects instructed in dietary management and treated with "anorectic" drugs, lose more weight on the average than those treated with placebo and diet, as determined in relatively short-term clinical trials.

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The possible origins of the increased weight loss due to the various drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related in part to variables other than the drugs prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss. The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks or months duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited. The bioavailability of **IONAMIN** has been studied in humans in which blood levels of phentermine were measured by a gas-chromatography method. Blood levels obtained with the 15 mg and 30 mg resin complex formulations indicated slower absorption with a reduced but prolonged peak concentration and without a significant difference in prolongation of blood levels when compared with the same doses of phentermine hydrochloride. The clinical significance of these differences is not known. In clinical trials establishing the efficacy of **IONAMIN**, a single daily dose produced an effect comparable to the produced by other regimens of "anorectic" drug therapy.

INDICATIONS AND CLINICAL USE

As a short-term (i.e. a few weeks) adjunct to continued dietary treatment in the medical management of obesity, in patients who have not responded to an appropriate weight reducing diet alone. IONAMIN (phentermine resin complex) is recommended only for obese 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., hypertension, diabetes, hyperlipidaemia).

The limited usefulness of agents of this class (see Actions, Clinical Pharmacology) should be measured against possible risk factors inherent in their use such as those described below.

BODY MASS INDEX (BMI), kg/m^2

	Height (feet, inches)					
Weight (pounds)	**5'0''**	**5'3''**	**5'6''**	**5'9''**	**6'0''**	**6'3''**
140	**27**	**25**	**23**	**21**	**19**	**18**
150	**29**	**27**	**24**	**22**	**20**	**19**
160	**31**	**28**	**26**	**24**	**22**	**20**
170	**33**	**30**	**28**	**25**	**23**	**21**
180	**35**	**32**	**29**	**27**	**25**	**23**
190	**37**	**34**	**31**	**28**	**26**	**24**
200	**39**	**36**	**32**	**30**	**27**	**25**
210	**41**	**37**	**34**	**31**	**29**	**26**
220	**43**	**39**	**36**	**33**	**30**	**28**
230	**45**	**41**	**37**	**34**	**31**	**29**
240	**47**	**43**	**39**	**36**	**33**	**30**
250	**49**	**44**	**40**	**37**	**34**	**31**

Patients with BMI values > may be candidates for IONAMIN therapy.
Patients with BMI values of 27 - 29 may be candidates for IONAMIN therapy if they also have a concomitant risk factor (*e.g.*, hypertension, diabetes, hyperlipidaemia).

CONTRAINDICATIONS

Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states.

Patients with a history of drug abuse.

During or within 14 days following the administration of monamine oxidase inhibitors (hypertensive crises may result).

Tricyclic antidepressant: hypertensive crises may result or cardiac arrhythmia.

WARNINGS

Primary Pulmonary Hypertension

ANOREXIGENS INCREASE THE RISK OF DEVELOPING PRIMARY PULMONARY HYPERTENSION, AN OFTEN FATAL DISORDER*.

Although phentermine was not identified, an epidemiological study has indicated that use of other anorexigens for longer than 3 months was associated with a 23-fold increase in the risk of developing Primary Pulmonary Hypertension (PPH). There was no significant increase in risk for persons who had used these agents for 3 months or less. Obesity itself (body mass index $\geq$ 30 kg/m^2) was also independently associated with an increase of about two-fold in the risk of developing PPH. In the general population, the yearly occurrence of PPH is estimated to be about 1-2 cases per 1,000,000 persons. Therefore, the estimated risk associated with the long-term use of anorexigen drugs is about 23-46 cases per million persons exposed per year. The study further suggested that the risk of PPH rises with increasing duration of use of these drugs. The effect of intermittent compared to continuous use of anorexigens on the risk of PPH has not been determined.

The onset or aggravation of exertional dyspnea, or unexplained symptoms of angina pectoris, syncope, or lower extremity edema suggest the possibility of occurrence of pulmonary hypertension. Under these circumstances, treatment should be immediately discontinued, and the patient should be evaluated for the possible presence of PPH.

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 etiology of these valvulopathies has not been established and their course in individuals after use of the drugs are stopped is unknown. There have been no reported cases from health care professionals to date of this valvular condition occurring with the use of phentermine alone.

If tolerance to the "anorectic" effect develops, the recommended dose should not be exceeded in an attempt to increase the effect: rather, the drug should be discontinued. **IONAMIN** (phentermine resin complex) 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.

When using CNS active agents, consideration must always be given to the possibility of adverse interactions with alcohol.

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*Abenhaim L. et al. New Engl J Med 1996; 335:609-616

Drug Dependence: **IONAMIN** is related chemically and pharmacologically to amphetamine (d-and dl-amphetamine) and other stimulant drugs that have been extensively abused. The possibility of abuse of **IONAMIN** should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamine (d- and dl-amphetamine) 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 some of these drugs to many times that 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. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Use of **IONAMIN** by women who are or may become pregnant requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: **IONAMIN** is not recommended for use in children under 12 years of age.

PRECAUTIONS

Caution is to be exercised in prescribing **IONAMIN** (phentermine resin complex) for patients with even mild hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of **IONAMIN** and the concomitant dietary regimen.

IONAMIN may decrease the hypotensive effect of adrenergic neuron blocking drugs. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS

Cardiovascular: Palpitation, tachycardia, elevation of blood pressure, primary pulmonary hypertension and/or regurgitant cardiac valvular disease (see Warnings).

Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely psychotic episodes at recommended doses with some drugs in this class.

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

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Manifestations of acute overdosage may include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states.
Fatigue and depression usually follow the central stimulation.

Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdosage of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma.

Management of acute **IONAMIN** (phentermine resin complex) intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates overdosage.

DOSAGE AND ADMINISTRATION

One capsule daily, before breakfast or 10-14 hours before retiring. For individuals exhibiting greater drug responsiveness, **IONAMIN** '15' will usually suffice. **IONAMIN** '30' is recommended for less responsive patients. **IONAMIN** is not recommended for use in children under 12 years of age.

Ionamin should be used for a duration of no more than a few weeks (see WARNINGS).

DOSAGE FORMS

Availability

IONAMIN 15: Each yellow and gray capsule contains: phentermine 15 mg as the cationic exchange resin complex. Non medicinal ingredients: calcium phosphate, D&C Yellow No. 10, FD&C Yellow No. 6, gelatin, iron oxide, lactose, magnesium stearate and titanium dioxide. Bottles of 100 capsules.

IONAMIN 30: Each yellow capsule contains: phentermine 30 mg as the cationic exchange resin complex. Non medicinal ingredients: calcium phosphate, D&C Yellow No. 10, FD&C Yellow No. 10, FD&C Yellow No. 6, gelatin, lactose, magnesium stearate, polacrilin potassium and titanium dioxide. Bottles of 100 and 400 capsules.