

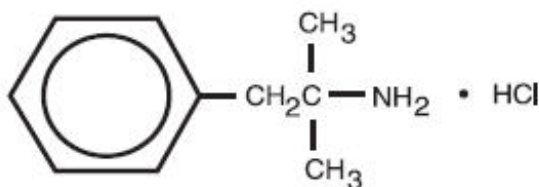
PHENTERMINE HYDROCHLORIDE - phentermine hydrochloride capsule
Blenheim Pharmacal, Inc.

PHENTERMINE HYDROCHLORIDE
CAPSULES, USP
CIV

Rx only

DESCRIPTION

Phentermine hydrochloride, USP has the chemical name of α,α -Dimethylphenethylamine hydrochloride. The structural formula is as follows:



$C_{10}H_{15}N \cdot HCl$

M.W. 185.69

Phentermine hydrochloride is a white, odorless, hygroscopic, crystalline powder which is soluble in water and lower alcohols; slightly soluble in chloroform and insoluble in ether.

Phentermine hydrochloride, an anorectic agent for oral administration, is available as:

- a) powder-filled capsules containing 30 mg phentermine hydrochloride (equivalent to 24 mg phentermine) and inactive ingredients: corn starch, magnesium stearate, lactose anhydrous. In addition, the natural/blue capsules contain gelatin, D&C Red # 28, and FD&C Blue # 1; the yellow/yellow capsules contain gelatin, D&C Yellow # 10, FD&C Red # 3, and titanium dioxide; and the black/black capsules contain gelatin, FD&C Yellow # 6, FD&C Blue # 1, and FD&C Red # 40. The imprinting ink for the natural/blue capsules and yellow/yellow capsules contains: shellac glaze in ethanol, iron oxide black, n-butyl alcohol, propylene glycol, ethanol, methanol, FD&C Blue # 2 Aluminum Lake, FD&C Red # 40 Aluminum Lake, FD&C Blue # 1 Aluminum Lake, and D&C Yellow # 10 Aluminum Lake. The imprinting ink for the black/black capsules contains: shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, strong ammonia solution, yellow iron oxide, and dimethicone.
- b) pellet-filled capsules containing 30 mg phentermine hydrochloride (equivalent to 24 mg phentermine) and inactive ingredients: sugar spheres, hypromellose, titanium dioxide, polyethylene glycol, polysorbate 80, FD&C Blue # 2 Aluminum Lake, FD&C Blue # 1, and gelatin. The imprinting ink for the pellet-filled capsules contains: shellac glaze in ethanol, iron oxide black, n-butyl alcohol, propylene glycol, ethanol, methanol, FD&C Blue # 2 Aluminum Lake, FD&C Red # 40 Aluminum Lake, FD&C Blue # 1 Aluminum Lake, and D&C Yellow # 10 Aluminum Lake.

CLINICAL PHARMACOLOGY

Phentermine is a sympathomimetic amine with pharmacologic activity similar to the prototype drugs of this class used in obesity, the amphetamines. 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 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, for example.

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' duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited.

INDICATIONS AND USAGE

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 $\geq 30 \text{ kg/m}^2$, or $\geq 27 \text{ kg/m}^2$ in the presence of other risk factors (e.g., hypertension, diabetes, hyperlipidemia).

Below is a chart of Body Mass Index (BMI) based on various heights and weights.

BMI is calculated by taking the patient's weight, in kilograms (kg), divided by the patient's height, in meters (m), squared. Metric conversions are as follows: pounds $\div 2.2 = \text{kg}$; inches $\times 0.0254 = \text{meters}$.

BODY MASS INDEX (BMI), kg/m²

weight (pounds)	Height (feet, inches)					
	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

The limited usefulness of agents of this class (see **CLINICAL PHARMACOLOGY**) should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS

Advanced arteriosclerosis, 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 monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS

Phentermine hydrochloride capsules are indicated only as short-term 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 selective serotonin reuptake inhibitors (e.g., fluoxetine, sertraline, fluvoxamine, paroxetine), have not been established. Therefore, coadministration of these drug products for weight loss is not recommended.

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.

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 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.

Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

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.

Usage with Alcohol

Concomitant use of alcohol with phentermine may result in an adverse drug interaction.

PRECAUTIONS

General

Caution is to be exercised in prescribing phentermine hydrochloride for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of phentermine and the concomitant dietary regimen.

Phentermine may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been performed with phentermine hydrochloride to determine the potential for carcinogenesis, mutagenesis or impairment of fertility.

Pregnancy

Teratogenic Effects

Pregnancy Category C

Animal reproduction studies have not been conducted with phentermine hydrochloride. It is also not known whether phentermine hydrochloride can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Phentermine should be given to a pregnant woman only if clearly needed.

Nursing Mothers

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.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Cardiovascular: Primary pulmonary hypertension and/or regurgitant cardiac valvular disease (see **WARNINGS**), palpitation, tachycardia, elevation of blood pressure.

Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely psychotic episodes at recommended doses.

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

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

DRUG ABUSE AND DEPENDENCE

Phentermine is related chemically and pharmacologically to the amphetamines. Amphetamines and related 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. 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 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.

OVERDOSAGE

Manifestations of acute overdosage with phentermine 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. Fatal poisoning usually terminates in convulsions and coma.

Management of acute phentermine 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 has been suggested for possible acute, severe hypertension, if this complicates phentermine overdosage.

DOSAGE AND ADMINISTRATION

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

Exogenous Obesity

The usual adult dosage is 15 to 30 mg at approximately 2 hours after breakfast for appetite control. Late evening medication should be avoided because of the possibility of resulting insomnia. Administration of one capsule (30 mg) daily has been found to be adequate in depression of the appetite for 12 to 14 hours.

Phentermine is not recommended for use in patients 16 years of age and under.

HOW SUPPLIED

Phentermine hydrochloride capsules are supplied as:

30 mg powder-filled capsules, natural/blue; imprinted logo LANNETT on the cap and 1308 on the body, in bottles of 100 (NDC 0527-1308-01) and 1000 (NDC 0527-1308-10) capsules.

30 mg powder-filled capsules, yellow/yellow; imprinted logo LANNETT on the cap and 1310 on the body, in bottles of 100 (NDC 0527-1310-01) and 1000 (NDC 0527-1310-10) capsules.

30 mg powder-filled capsules, black/black; imprinted logo LANNETT on the cap and logo 0597 logo on the body, in bottles of 100 (NDC 0527-0597-01) and 1000 (NDC 0527-0597-10) capsules.

30 mg pellet-filled capsules, blue/white; imprinted logo LANNETT on the cap and 1438 on the body, in bottles of 100 (NDC 0527-1438-01) and 1000 (NDC 0527-1438-10) capsules.

Storage

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Protect from moisture.

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

Manufactured by:

LANNETT COMPANY, INC.

Philadelphia, PA 19136

Made in the USA

Revised 03/10

10-532

Bottle Label 10544-593-28



PHENTERMINE HYDROCHLORIDE

phentermine hydrochloride capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:10544-593(NDC:0527-1308)
Route of Administration	ORAL	DEA Schedule	CIV

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
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Phentermine Hydrochloride (UNII: 0K2I5050TV) (Phentermine - UNII:C045TQL4WP)	Phentermine Hydrochloride	30 mg
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Inactive Ingredients

Ingredient Name	Strength
Starch, Corn (UNII: O8232NY3SJ)	
Magnesium stearate (UNII: 70097M6I30)	
Anhydrous lactose (UNII: 3SY5LH9PMK)	
Gelatin (UNII: 2G86QN327L)	
D&C Red NO. 28 (UNII: 767IP0Y5NH)	
FD&C Blue NO. 1 (UNII: H3R47K3TBD)	
shellac (UNII: 46N107B71O)	
Ferrosoferric Oxide (UNII: XM0M87F357)	
butyl alcohol (UNII: 8PJ61P6TS3)	
Propylene glycol (UNII: 6DC9Q167V3)	
Alcohol (UNII: 3K9958V90M)	
Methyl Alcohol (UNII: Y4S76JWI15)	
FD&C Blue NO. 2 (UNII: L06K8R7DQK)	
FD&C Red NO. 40 (UNII: WZB9127XOA)	
D&C Yellow NO. 10 (UNII: 35SW5USQ3G)	
Aluminum Oxide (UNII: LMI26O6933)	

Product Characteristics

Color	blue (Natural/blue)	Score	no score
Shape	CAPSULE	Size	16mm
Flavor		Imprint Code	LANNETT;1308
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10544-593-28	28 in 1 BOTTLE		
2	NDC:10544-593-30	30 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA087022	03/04/2010	

Labeler - Blenheim Pharmacal, Inc. (171434587)

Registrant - Blenheim Pharmacal, Inc. (171434587)

Establishment

Name	Address	ID/FEI	Business Operations
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Revised: 8/2010

Blenheim Pharmacal, Inc.