AD1-40091

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ADIPEX-P® safely and effectively. See full prescribing information for ADIPEX-P®.

ADIPEX-P® (phentermine hydrochloride) tablets, for oral use CIV

INDICATIONS AND USAGE
ADIPEX-P® is a sympathomimetic amine anorectic indicated as a short-term adjunct (a few weeks) in the 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 greater than or equal to 30 kg/m², or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia). (1) The limited usefulness of agents of this class, including ADIPEX-P®, should be measured against possible risk factors inherent in their use. (1)

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Revised: 9/2020

*Sections or subsections omitted from the full prescribing information are not listed.
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Below is a chart of body mass index (BMI) based on various heights and weights.

**BMI Chart**

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<tr>
<th>Height (feet, inches)</th>
<th>Weight (pounds)</th>
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The limited usefulness of agents of this class, including ADIPEX-P®, [see Clinical Pharmacology (12.1, 12.2)] should be measured against possible risk factors inherent in their use such as those described below.

2 DOSAGE AND ADMINISTRATION
2.1 Exogenous Obesity
Dosage should be individualized to obtain an adequate response with the lowest effective dose. The usual adult dose is one capsule (37.5 mg) daily, or half tablets (18.75 mg) twice daily, as prescribed by the physician, administered before breakfast or 1 to 2 hours after breakfast for appetite control. The usual adult dose is one tablet (315 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.

ADIPEX-P® is not recommended for use in pediatric patients less than or equal to 16 years of age. Late evening medication should be avoided because of the possibility of resulting insomnia.

2.2 Dosage in Patients With Renal Impairment
The recommended maximum dosage of ADIPEX-P® is 15 mg daily for patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m²), 12.5 mg daily for patients with eGFR less than 15 mL/min/1.73 m² or end-stage renal disease requiring dialysis [see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)].

3 DOSAGE FORMS AND STRENGTHS
Capsules: 37.5 mg phentermine hydrochloride, USP (equivalent to 30 mg phentermine base). Tablets: 315 mg phentermine hydrochloride, USP (equivalent to 30 mg phentermine base).

4 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 [see Use in Specific Populations (8.1)]
• Nursing [see Use in Specific Populations (8.3)]
• Known hypersensitivity, or idiosyncrasy to the sympathomimetic amines

5 WARNINGS AND PRECAUTIONS
5.1 Coadministration With Other Drug Products for Weight Loss
ADIPEX-P® is indicated only as short-term (a few weeks) monotherapy for the management of exogenous obesity. The safety and efficacy of combination therapy with ADIPEX-P® 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 ADIPEX-P® and these drug products is not recommended.

5.2 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 ADIPEX-P® 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.

6 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)]

7 DRUG INTERACTIONS
7.1 Monoamine Oxidase Inhibitors
Use of ADIPEX-P® is contraindicated during or within 14 days following the administration of monoamine oxidase inhibitors because of the risk of hypertensive crisis.

7.2 Alcohol
Concomitant use of alcohol with ADIPEX-P® may result in an adverse drug reaction.

7.3 Insulin and Oral Hypoglycemic Medications
Requirements may be altered [see Warnings and Precautions (5.5)].

7.4 Adrenergic Neuron Blocking Drugs
ADIPEX-P® may decrease the hypertensive effect of adrenergic neuron blocking drugs.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
ADIPEX-P® 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 dl-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.

8.2 Alcohol
It is not known if ADIPEX-P® 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.

8.3 Pediatric Use
Safety and effectiveness in pediatric patients have not been established. Because pediatric obesity is a chronic condition requiring long-term treatment, the use of this product, approved for short-term therapy, is not recommended.

8.4 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.

8.6 Renal Impairment

Based on the reported excretion of phentermine in urine, exposure increases can be expected in patients with renal impairment [see Clinical Pharmacology (12.3)]. Use caution when administering ADIPEX-P® to patients with renal impairment. In patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m²), the limit of dosage of ADIPEX-P® to 15 mg daily (see Dosage and Administration (2.2)). ADIPEX-P® has not been studied in patients with eGFR less than 15 mL/min/1.73 m², including end-stage renal disease requiring dialysis; avoid use in these populations.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Phentermine is a Schedule IV controlled substance.

9.2 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.

9.3 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 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. A severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

10 OVERDOSAGE

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

10.1 Acute Overdose

Manifestations of acute overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, and panic states. Fatigue and depression usually follow the possibility of overdosage. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose.

10.2 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 intoxication is psychosis, often clinically indistinguishable from schizophrenia. See Drug Abuse and Dependence (9.3).

11 DESCRIPTION

Phentermine hydrochloride, USP is a sympathomimetic amine anorectic. It has the chemical name of \( \text{C}_{10}\text{H}_{15}\text{N} \cdot \text{HCl} \). Dimethylphenethylamine hydrochloride. The structural formula is as follows:

![Chemical structure of phentermine](image)

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

ADIPEX-P®, an anorectic agent for oral administration, is available as a capsule or tablet containing 375 mg of phentermine hydrochloride, USP (equivalent to 30 mg of phentermine base).

ADIPEX-P® Capsules contain the inactive ingredients black iron oxide, corn starch, D&C Red #3, FD&C Blue #1, gelatin, lactose monohydrate, magnesium stearate, propylene glycol, shellac, and titanium dioxide.

ADIPEX-P® Tablets contain the inactive ingredients corn starch, lactose (anhydrous), magnesium stearate, microcrystalline cellulose, pregelatinized corn starch, and sucrose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ADIPEX-P® is a sympathomimetic amine with pharmacologic activity similar to the prototype drugs of this class used in obesity, amphetamine (d- and dl-amphetamine). Drugs of this class used in obesity are commonly known as “anorectics” or “anorexigenics.” It has not been established that the primary action of such drugs in treating obesity is one of appetite suppression since other central nervous system actions, or metabolic effects, may also be involved.

12.2 Pharmacodynamics

Typical actions of amphetamines 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.

12.3 Pharmacokinetics

Following the administration of phentermine, phentermine reaches peak concentrations \( C_{\text{max}} \) after 3.0 to 4.4 hours.

Drug Interactions

In a single-dose study comparing the exposures after oral administration of a combination capsule of 15 mg phentermine and 92 mg topiramate to the exposures after oral administration of a 15 mg phentermine capsule or a 92 mg topiramate capsule, there is no significant topiramate exposure change in the presence of phentermine. However, in the presence of topiramate, phentermine \( C_{\text{max}} \) and AUC increase 13% and 42%, respectively.

Specific Populations

Renal Impairment

Cumulative urinary excretion of phentermine under uncontrolled urinary pH conditions was 52% to 85%.

Systemic exposure of phentermine may increase up to 91%, 45%, and 22% in patients with severe, moderate, and mild renal impairment, respectively [see Dosage and Administration (2.2) and Use in Specific Populations (8.6)].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

14 CLINICAL STUDIES

No clinical studies have been conducted with ADIPEX-P®. In relatively short-term clinical trials, adult obese subjects instructed in dietary management and treated with “anorectic” drugs lost more weight on the average than those treated with placebo and diet. 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 over several 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.

16 HOW SUPPLIED/STORAGE AND HANDLING

ADIPEX-P® Capsules and Tablets are available for oral administration containing 375 mg phentermine hydrochloride, USP (equivalent to 30 mg phentermine base). Each white, blographed, scored tablet is debossed with “ADIPEX-P®” and “P.” Tablets are packaged in bottles of 100 (NDC 57844-140-50) and 1000 (NDC 57844-140-01).

Each capsule has an opaque white body and an opaque blue cap. Each capsule is imprinted with “ADIPEX-P® - 315” on the cap and two stripes on the body using dark blue ink. Capsules are packaged in bottles of 100 (NDC 57644-019-01). Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

17 PATIENT COUNSELING INFORMATION

Patients must be informed that ADIPEX-P® is 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, and that coadministration of phentermine with other drugs for weight loss is not recommended [see Indications and Usage (1) and Warnings and Precautions (5)].

Patients must be instructed on how much ADIPEX-P® to take, and when and how to take it [see Dosage and Administration (2)].

Advise pregnant women and nursing mothers not to use ADIPEX-P® [see Use in Specific Populations (8.1, 8.3)].

Patients must be informed about the risks of use of phentermine (including the risks discussed in Warnings and Precautions), about the symptoms of potential adverse reactions and when to contact a physician and/or take other action. The risks include, but are not limited to:

- Development of primary pulmonary hypertension [see Warnings and Precautions (5.2)]
- Development of serious valvular heart disease [see Warnings and Precautions (5.3)]
- Effects on the ability to engage in potentially hazardous tasks [see Warnings and Precautions (5.5)]
- The risk of an increase in blood pressure [see Warnings and Precautions (5.8) and Adverse Reactions (6)]
- The risk of interactions [see Contraindications (4), Warnings and Precautions (5) and Drug Interactions (7)]
- See also, for example, Adverse Reactions (6) and Use in Specific Populations (8).

The patients must also be informed about

- the potential for developing tolerance and actions if they suspect development of tolerance [see Warnings and Precautions (5.4)]
- the risk of development and the potential consequences of abuse [see Warnings and Precautions (5.6), Drug Abuse and Dependence (9), and Overdosage (10)].

Tell patients to keep ADIPEX-P® in a safe place to prevent theft, accidental overdose, misuse or abuse. Selling or giving away ADIPEX-P® may harm others and is against the law.

Brands listed are the trademarks of their respective owners.

Manufactured in Croatia By:
Pliva Hrvatska d.o.o.
Zagreb, Croatia

Manufactured For:
Teva Pharmaceuticals USA, Inc.
Parsippany, NJ 07054
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