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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**DOSEAGE AND ADMINISTRATION**

- Dosage should be individualized to obtain an adequate response with the lowest effective dose. (2.1)
- Late evening administration should be avoided (risk of insomnia). (2.1)
- ADIPEX-P® should not be taken with or without food. (2.1)
- Limit the dosage to 15 mg daily for patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m²). (2.2)

**DOSEAGE FORMS AND STRENGTHS**

- Capsules containing 37.5 mg phentermine hydrochloride. (3)
- Tablets containing 37.5 mg phentermine hydrochloride. (3)

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**CONTRAINDICATIONS**

- History of cardiovascular disease (e.g., coronary artery disease, stroke, arrhythmias, congestive heart failure, uncontrolled hypertension) (4)
- During or within 14 days following the administration of monoamine oxidase inhibitors (4)
- Hyperthyroidism (4)
- Glaucoma (4)
- History of drug abuse (4)

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**WARNINGS AND PRECAUTIONS**

- Coadministration with other drugs for weight loss is not recommended (safety and efficacy of combination not established). (5.1)
- Recent cases of primary pulmonary hypertension have been reported. ADIPEX-P® should be discontinued in case of new, unexplained symptoms of dyspnea, angina pectoris, syncope or lower extremity edema. (5.2)
- Rare cases of serious regurgitant cardiac valvular disease have been reported. (5.3)
- Tolerance to the anorectic effect usually develops within a few weeks. If this occurs, ADIPEX-P® should be discontinued. The recommended dose should not be exceeded. (5.4)
- ADIPEX-P® may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle. (5.5)
- Risk of abuse and dependence. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. (5.6)
- Concomitant alcohol use may result in an adverse drug reaction. (5.7)
- Use caution in patients with even mild hypertension (risk of increase in blood pressure). (5.8)
- A reduction in dose of insulin or oral hypoglycemic medication may be required in some patients. (5.9)

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**ADVERSE REACTIONS**

Adverse events have been reported in the cardiovascular, central nervous, gastrointestinal, allergic, and endocrine systems. (6)

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**ADVERSE DRUG INTERACTIONS**

- Monoamine oxidase inhibitors: Risk of hypertensive crisis. (4, 7.1)
- Alcohol: Consider potential interaction (7.2)
- Insulin and oral hypoglycemics: Requirements may be altered. (7.3)
- Adrenergic neuron blocking drugs: Hypotensive effect may be increased by ADIPEX-P®. (7.4)

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**USE IN SPECIFIC POPULATIONS**

- Nursing mothers: Discontinue drug or nursing taking into consideration importance of drug to mother. (4, 8.3)
- Pediatric use: Safety and effectiveness not established. (8.4)
- Geriatric use: Due to substantial renal excretion, use with caution. (8.5)
- Renal Impairment: Avoid use in patients with eGFR less than 15 mL/min or end-stage renal disease requiring dialysis. (8.6)

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**FULL PRESCRIBING INFORMATION:**

**INDICATIONS AND USAGE**

ADIPEX-P® is a sympathomimetic amine anorectic indicated as a short-term (a few weeks) 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)

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**

- Risk of abuse and dependence. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of over dosage. (5.6)
- Concomitant alcohol use may result in an adverse drug reaction. (5.7)
- Use caution in patients with even mild hypertension (risk of increase in blood pressure). (5.8)
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**HIGHLIGHTS OF PRESCRIBING INFORMATION**

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- Concomitant alcohol use may result in an adverse drug reaction. (5.7)
- Use caution in patients with even mild hypertension (risk of increase in blood pressure). (5.8)
- A reduction in dose of insulin or oral hypoglycemic medication may be required in some patients. (5.9)

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- Concomitant alcohol use may result in an adverse drug reaction. (5.7)
- Use caution in patients with even mild hypertension (risk of increase in blood pressure). (5.8)
- A reduction in dose of insulin or oral hypoglycemic medication may be required in some patients. (5.9)
5 WARNINGS AND PRECAUTIONS
5.1 Coadministration With Other Drug Products for Weight Loss
ADIPLEX-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 ADIPLEX-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, paroxetine), have not been established. Therefore, coadministration of ADIPLEX-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 ADIPLEX-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. Other initial symptoms may 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.

5.3 Valvular Heart Disease
Serious regurgitant cardiacovalvular disease, primarily affecting the mitral 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 ADIPLEX-P® alone cannot be ruled out; there have been rare cases of valvular heart disease in patients who reportedly have taken phentermine alone.

5.4 Development of Tolerance, Discontinuation in Case of Tolerance
When tolerance to the anorectic effect develops, the recommended dosage should not be increased in an attempt to increase the effect; rather, the drug should be discontinued.

5.5 Effect on the Ability to Engage in Potentially Hazardous Tasks
ADIPLEX-P® 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.

5.6 Risk of Abuse and Dependence
ADIPLEX-P® is related chemically and pharmacologically to amphetamine (d- and d,l-amphetamine) and to other related stimulant drugs that have been extensively abused. The possibility of abuse of ADIPLEX-P® 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 Overdose (10). The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose.

5.7 Usage With Alcohol
Concomitant use of alcohol with ADIPLEX-P® may result in an adverse drug reaction.

5.8 Use in Patients With Hypertension
Use caution in prescribing ADIPLEX-P® for patients with even mild hypertension (risk of increase in blood pressure).

5.9 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.

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 effect following prolonged high dosage administration [see Drug Abuse and Dependence (9.3)]

The following adverse reactions to phentermine have reportedly occurred in patients receiving a combination of phentermine with fenfluramine or dexfenfluramine:

• Weight gain
• Skin rash
• Abdominal cramps
• Headache
• Insomnia
• Anxiety

7 DRUG INTERACTIONS
7.1 Monoamine Oxidase Inhibitors
Use of ADIPLEX-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 ADIPLEX-P® may result in an adverse drug reaction.

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

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

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category X
ADIPLEX-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. Phenetermine 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.

8.3 Nursing Mothers
It is not known if ADIPLEX-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.

8.4 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.

8.5 Geriatric Use
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosage 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 phenetermine in urine, exposure increases can be expected in patients with renal impairment [see Clinical Pharmacology (12.9)].

Use caution when administering ADIPLEX-P® to patients with renal impairment. In patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m²), limit the dosage of ADIPLEX-P® to 15 mg daily [see Dosage and Administration (2.1)]. ADIPLEX-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 Overdosage
Manifestations of acute overdose include restlessness, tremor, hyperpyrexia, rapid respiration, confusion, assaultiveness, hallucinations, and panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include tachycardia, arrhythmia, hypotension or hypertension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea and abdominal cramps. Overdose 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 hemo-dialysis and 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 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 drug. It has the chemical name of α-, α, β-Dimethylphenylalanine hydrochloride, the structural formula is as follows:

\[
\begin{align*}
\text{C}_9\text{H}_{13}\text{NCl} & \quad \text{HCl} \\
\text{CH}_3 & \quad \text{NH}_2 & \quad \text{Cl} \\
\text{CH}_3 & \quad \text{H} \\
\text{H} & \\
\text{H} & \\
\text{H} & \quad \text{Cl} \\
\end{align*}
\]

M.W. 185.7

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. ADIPLEX-P®, an anorectic agent for oral administration, is available as a capsule or tablet containing 37.5 mg of phentermine hydrochloride (equivalent to 30 mg of phentermine base).

ADIPEX-P® Capsules contain the inactive ingredients Black Iron Oxide, Corn Starch, D&C Red #33, FD&C
Blue #1. Gelatin, Lactose Monohydrate, Magnesium Stearatate, Propylene Glycol, Shellac, and Titanium Dioxide.

ADIPEX-P® Tablets contain the inactive ingredients Corn Starch, Lactose (Anhydrous), Magnesium Stearate, Micro-crystalline Cellulose, Pregelatinized Starch, Sucrose, and FD&C Blue #1.

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. Tachyphyaxis 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 (Cmax) after 3.0 to 4.4 hours.

Drug Interactions
In a singledose 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 topramate, phentermine Cmax and AUC increase 13% and 42%, respectively.

Specific Populations
Renal Impairment
Cumulative urinary excretion of phentermine under uncontrolled urinary pH conditions was 62% 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
Available in tablets and capsules containing 37.5 mg phentermine hydrochloride (equivalent to 30 mg phentermine base). Each blue and white, oblong, speckled, scored tablet is debossed with “ADIPEX-P®” and “37.5”. The #3 capsule has an opaque white body and an opaque bright blue cap. Each capsule is imprinted with “ADIPEX-P®” - “37.5” on the cap and two stripes on the body using dark blue ink.

AD1-40062

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)].

Adverse reactions and when to contact a physician and/or pharmacist should be reviewed. The risks include, but are not limited to:

• 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) and Adverse Reactions (6)]
• the risk of dependence 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.

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Manufactured In Croatia By:
Pliva Hrvatska d.o.o.
Zagreb, Croatia
Manufactured For:
Teva Select Brands, Horsham, PA 19044
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