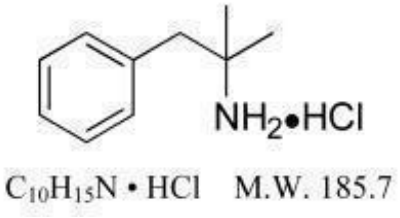
LOMAIRA- phentermine hydrochloride tablet
KVK-TECH, INC.

LOMAIRA™ (phentermine hydrochloride USP) tablets, CIV

DESCRIPTION

Phentermine hydrochloride is a sympathomimetic amine anorectic. Its chemical name is α,α,-dimethylphenethylamine hydrochloride. The structural formula is as follows:



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

LOMAIRA™ tablet is available as an oral tablet containing 8 mg of phentermine hydrochloride (equivalent to 6.4 mg of phentermine base). Each LOMAIRA™ tablet also contains the following inactive ingredients: Corn Starch, Magnesium Stearate, NF, Microcrystalline Cellulose 102, NF, Stearic Acid, NF, FD&C Blue #1, Sucrose and Pharmaceutical Glaze.

CLINICAL PHARMACOLOGY

Mechanism of Action

Phentermine is a sympathomimetic amine with pharmacologic activity similar to the prototype drugs of this class used in obesity, amphetamine (d- and dll-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.

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.

Pharmacokinetics

Specific Populations

Renal Impairment

Phentermine was not studied in patients with renal impairment. The literature reported cumulative urinary excretion of phentermine under uncontrolled urinary pH conditions is 62%-85%. Exposure increases can be expected in patients with renal impairment. Use caution when administering phentermine to patients with renal impairment.

CLINICAL STUDIES

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.

INDICATIONS AND USAGE

LOMAIRA™ tablets are 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 in patients with an initial body mass index greater than or equal to 30 kg/m^2, or greater than or equal to 27 kg/m^2 in the presence of other risk factors (e.g., controlled 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 ÷ 2.2 = kg; inches x 0.0254 = meters.

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

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

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 *Precautions*)
• Nursing (see *Precautions*)
• Known hypersensitivity, or idiosyncrasy to the sympathomimetic amines

WARNINGS

Coadministration with Other Drug Products for Weight Loss

LOMAIRA™ 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 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.

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 dll-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 *Adverse Reactions/ Drug Abuse and Dependence* and *Overdosage*.

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

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.

PRECAUTIONS

Information for Patients

Patients must be informed that phentermine hydrochloride 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* and *Warnings*).

Patients must be instructed on how much phentermine to take, and when and how to take it (see *Dosage and Administration*).

Advise pregnant women and nursing mothers not to use phentermine (see *Precautions*).

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*)
• Development of serious valvular heart disease (see *Warnings*)
• Effects on the ability to engage in potentially hazardous tasks (see *Warnings*)
• The risk of an increase in blood pressure (see *Warnings* and *Adverse Reactions*)
• The risk of interactions (see *Contraindications*, *Warnings*, and *Precautions/ Drug Interactions*)

The patients must also be informed about

• the potential for developing tolerance and actions if they suspect development of tolerance (see *Warnings*) and
• the risk of dependence and the potential consequences of abuse (see *Warnings*, *Drug Abuse and Dependence*, and *Overdosage*).

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

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*)

Adrenergic Neuron Blocking Drugs

Phentermine may decrease the hypotensive effect of adrenergic neuron blocking drugs.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Pregnancy

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 dll-amphetamine) (see *Clinical Pharmacology*). 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.

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.

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*).

ADVERSE REACTIONS

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

- Primary pulmonary hypertension (see *Warnings*)

- Valvular heart disease (see *Warnings*)

- Effect on the ability to engage in potentially hazardous tasks (see *Warnings*)

- Withdrawal effects following prolonged high dosage administration (see *Drug Abuse and Dependence*)

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 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.

OVERDOSAGE

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

Acute Overdosage

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

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*.

DOSAGE AND ADMINISTRATION

Dosage should be individualized to obtain an adequate response with the lowest effective dose. The usual adult dose is one tablet three times a day ½ hour before meals. This tablet is scored to facilitate administering one half of the usual dosage for patients not requiring the full dose. Phentermine hydrochloride 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.

HOW SUPPLIED/STORAGE AND HANDLING

LOMAIRA™ is available as follows:

LOMAIRA™ 8 mg is supplied as white butterfly shaped tablets with blue speckles, debossed “K1” on one side and bisected on the other side.

Bottles of 30, NDC 10702-001-03

Bottles of 60, NDC 10702-001-06

Bottles of 90, NDC 10702-001-09

Bottles of 250, NDC 10702-001-25

Bottles of 500, NDC 10702-001-50

Bottles of 1000, NDC 10702-001-10

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

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

Keep out of the reach of children.

Manufactured by:
KVK-Tech, Inc.
110 Terry Drive
Newtown, PA 18940

Item ID# 006178/07

Manufacturer’s Code: 10702 09/16

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

30 Tablets

NDC 10702- **001**-03

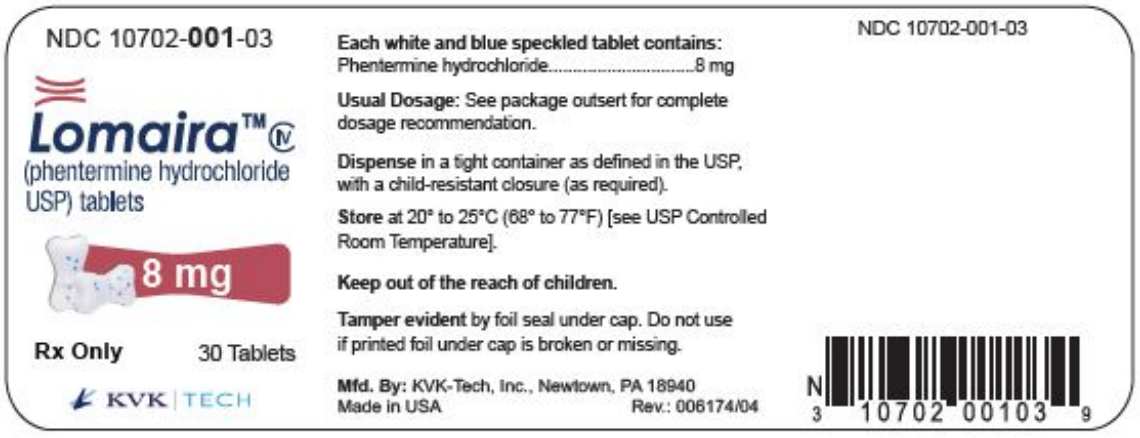
LOMAIRA ™ CIV

(phentermine hydrochloride USP) tablets

8 mg

30 Tablets Rx Only

KVK-TECH, INC.



60 Tablets

NDC 10702- **001**-06

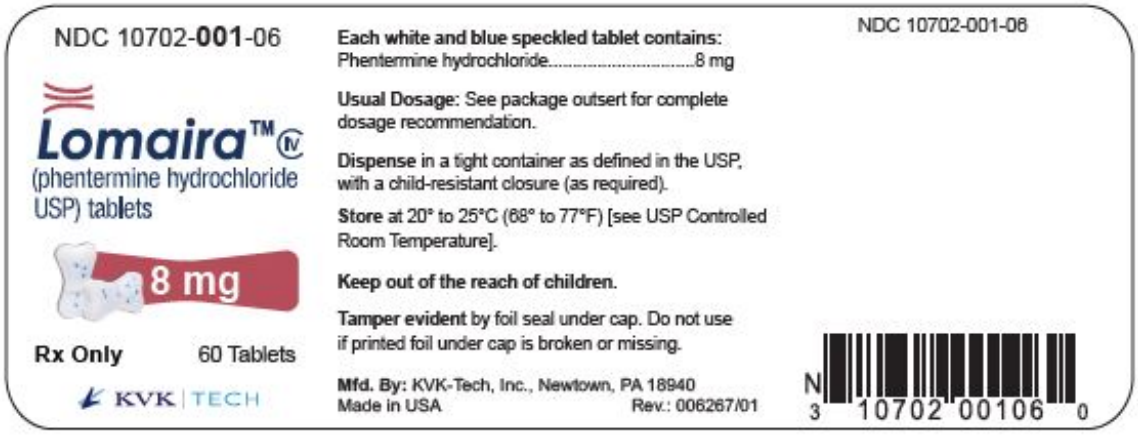
LOMAIRA ™ CIV

(phentermine hydrochloride USP) tablets

8 mg

60 Tablets Rx only

KVK-TECH, INC.



90 Tablets

NDC 10702- **001**-09

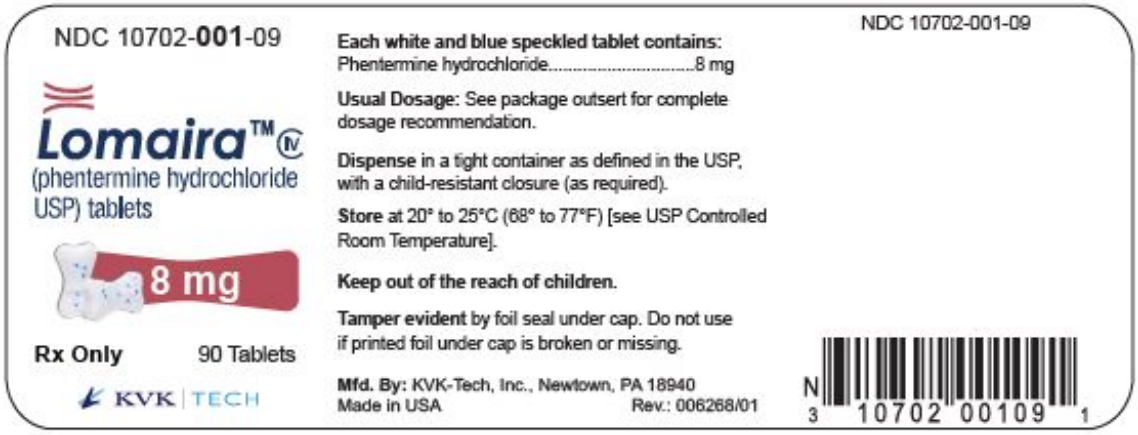
LOMAIRA ™ CIV

(phentermine hydrochloride USP) tablets

8 mg

90 Tablets Rx only

KVK-TECH, INC.



250 Tablets

NDC 10702- **001**-25

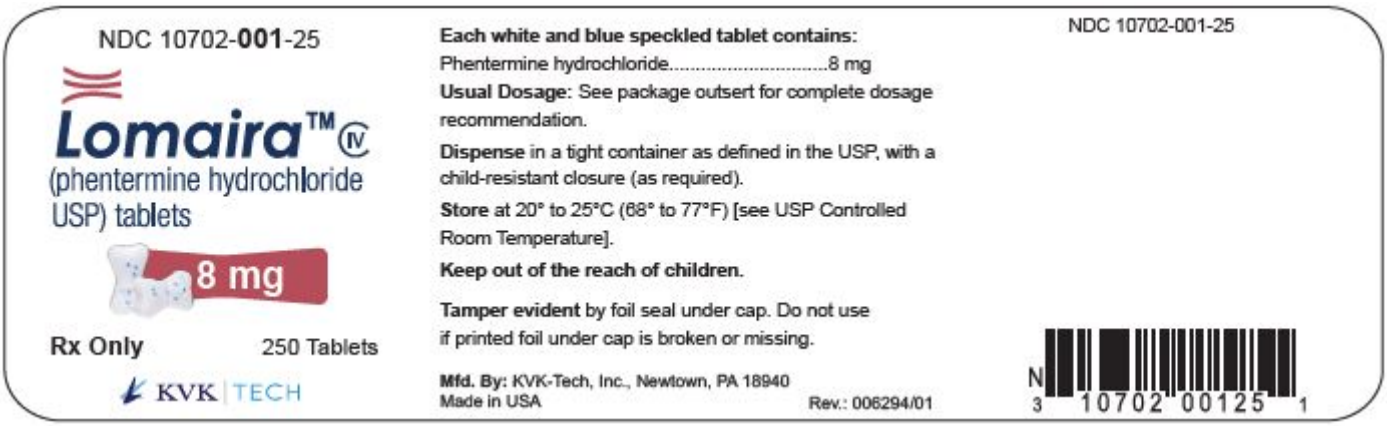
LOMAIRA ™ CIV

(phentermine hydrochloride USP) tablets

8 mg

250 Tablets Rx only

KVK-TECH, INC.



500 Tablets

NDC 10702- **001**-50

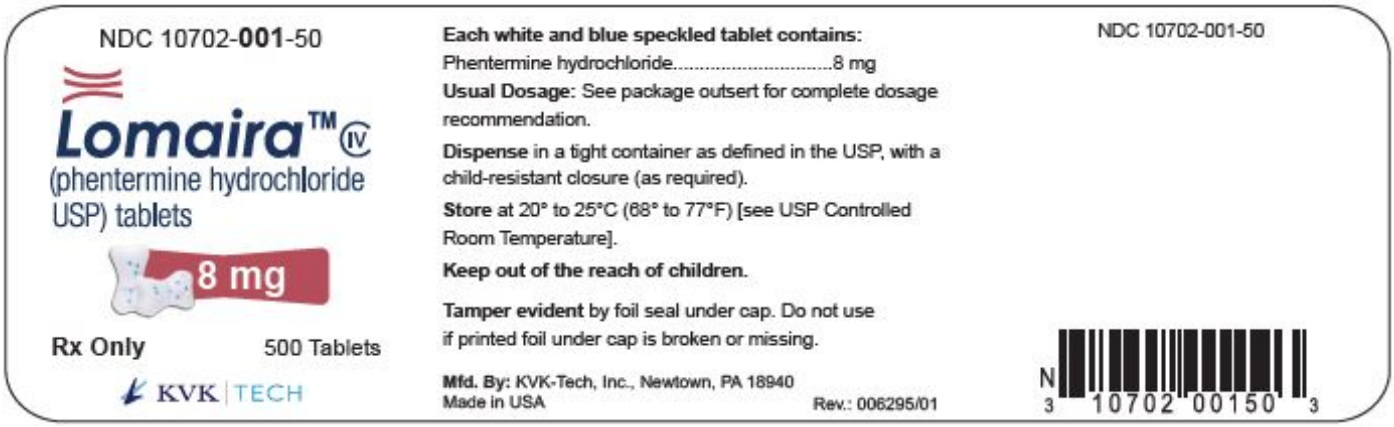
LOMAIRA ™ CIV

(phentermine hydrochloride USP) tablets

8 mg

500 Tablets Rx only

KVK-TECH, INC.



1000 Tablets

NDC 10702-001-10

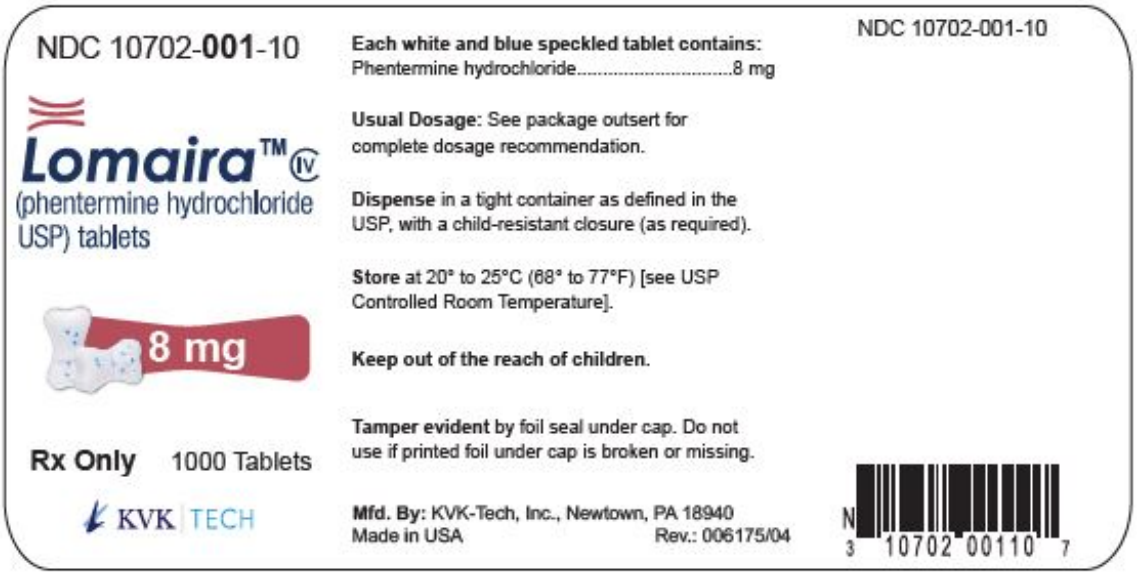
LOMAIRA ™ CIV

(phentermine hydrochloride USP) tablets

8 mg

Rx only 1000 Tablets

KVK-TECH, INC.



LOMAIRA

phentermine hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:10702-001
Route of Administration	ORAL	**DEA Schedule**	CIV

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
PHENTERMINE HYDROCHLORIDE (UNII: 0K2I505OTV) (PHENTERMINE - UNII:C045TQL4WP)	PHENTERMINE HYDROCHLORIDE	8 mg

Inactive Ingredients	
Ingredient Name	**Strength**
STARCH, CORN (UNII: O8232NY3SJ)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
SUCROSE (UNII: C151H8M554)	

Product Characteristics			
Color	white, blue (Speckles)	**Score**	2 pieces
Shape	FREEFORM (Butterfly Shape)	**Size**	3mm
Flavor		**Imprint Code**	K;1
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10702-001-03	30 in 1 BOTTLE; Type 0: Not a Combination Product	09/12/2016	
2	NDC:10702-001-06	60 in 1 BOTTLE; Type 0: Not a Combination Product	09/12/2016	
3	NDC:10702-001-09	90 in 1 BOTTLE; Type 0: Not a Combination Product	09/12/2016	
4	NDC:10702-001-25	250 in 1 BOTTLE; Type 0: Not a Combination Product	09/12/2016	
5	NDC:10702-001-50	500 in 1 BOTTLE; Type 0: Not a Combination Product	09/12/2016	
6	NDC:10702-001-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	09/12/2016	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203495	09/12/2016	

Labeler - KVK-TECH, INC. (173360061)

Registrant - AVANTHI INC. (832316694)

Establishment

Name	Address	ID/FEI	Business Operations
KVK-TECH, INC.		173360061	manufacture(10702-001)

Revised: 12/2018 KVK-TECH, INC.