

**LACHMAN CONSULTANT SERVICES, INC.**  
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

1600 STEWART AVENUE, WESTBURY, NY 11590  
(516) 222-6222 • FAX (516) 683-1887

0009 5 OCT -3 P1:55

September 30, 2005

Division of Dockets Management  
Food and Drug Administration – HFA-305  
Department of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Dear Sir or Madam:

**CITIZEN PETITION**

The undersigned, on behalf of a client, submits this petition in quadruplicate under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. § 355(j)(2)(C), and 21 C.F.R. §§ 10.20, 10.30, and 314.93, to request that the Commissioner of Food and Drugs make a determination that an Abbreviated New Drug Application (ANDA) may be submitted for Benzphetamine Hydrochloride Capsules, 50 mg.

**A. Action Requested**

The petitioner requests that the Commissioner of Food and Drugs make a determination that a Benzphetamine Hydrochloride Capsule, 50 mg drug product is suitable for submission as an ANDA. The reference-listed drug (RLD) product upon which this petition is based is Didrex® (Benzphetamine Hydrochloride) Tablets, 50 mg. The listing reference drug products, NDA No. 12-427, which is held by Pharmacia and Upjohn, appears in the electronic Orange Book, Approved Drug Products with Therapeutic Equivalence Evaluations 25<sup>th</sup> Edition (accessed September 30, 2005). A copy of that listing is provided in **Attachment A**. This petition requests a change in the dosage form, from tablet to capsule.

**B. Statement of Grounds**

Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act provides for the submission of an ANDA for a new drug that differs in dosage form from a listed drug, provided that the FDA has approved a petition seeking permission to file such an application.

The proposed change in dosage form, from a tablet to a capsule, is designed to provide a more convenient dosage form for those adult patients that find it difficult to swallow tablets. According to the labeling of the reference-listed drug products, the average dosage of Didrex® is "50 mg". The package insert for Didrex® (Benzphetamine Hydrochloride Tablets, 50 mg) is provided in **Attachment B** of this petition. The dosage for the proposed product is "50 mg". This dosage is consistent with that stated in the approved labeling of the reference listed drug product.

In summary, the proposed change in dosage form from that of the reference-listed drug (i.e., a change from a tablet to a capsule), will not affect the product's safety or efficacy. The indication

remains unchanged and the proposed dosing is the same as the dosing recommendations in the approved labeling for the reference-listed drug. Therefore, the Agency should conclude that clinical investigations are not necessary to demonstrate the proposed product's safety or effectiveness.

The proposed labeling for Benzphetamine Hydrochloride Capsules, 50 mg is included as **Attachment C**. Labeling for the proposed product will be consistent with the approved labeling for Didrex<sup>®</sup> (Benzphetamine Hydrochloride Tablets, 50 mg).

### **Pediatric Waiver Request**

In December of 2003, Congress passed the Pediatric Research Equity Act of 2003 that amended the Federal Food, Drug and Cosmetic Act to provide the Agency authority to require drug firms to study certain drugs in pediatric patients, if the Agency felt that such study would provide beneficial health data for that patient population. The Act also provided a provision for a waiver from such requirement if:

(iii) the drug or biological product —

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(II) is not likely to be used in a substantial number of pediatric patients.

The petitioner hereby requests that a waiver from the conduct of pediatric studies be granted for the approval of this petition to permit a subsequent ANDA filing. The drug product Benzphetamine does not appear on the historical list of drugs for which additional information may produce benefits in the pediatric population.

Based on the use and nature of the RLD, the proposed change in dosage form to a capsule from a tablet will not make the product any more likely to be used in pediatric patients. In addition, the limitations of use, i.e., 12 years of age and older, described in the labeling of the RLD make it unlikely that the proposed product would be used in a substantial number of pediatric patients other than those for which the product is currently indicated. Current available IMS data show that an average of about 138 prescriptions/month were dispensed to pediatric patients, which is a total of about 1656 prescriptions **per year**. While these data do not break out the number of prescriptions by age (range from 10 – 19 years), it is assumed that most are related to pediatric patients for whom this drug is labeled, i.e., patients from 12 years of age or older. However, even if some of all or the prescriptions are written for patients below 12 years of age, it appears that it is a small percentage of the 1656 prescriptions IMS reported and is far below the 50,000-prescription threshold cited in previous FDA documents, as a barometer to determine if the product would likely be used in a significant number of pediatric patients.

For the aforementioned reasons, the undersigned requests that the Commissioner grant this petition and authorize submission of an ANDA for Benzphetamine Hydrochloride Capsules, 50 mg.

**C. Environmental Impact**

According to 21 C.F.R. § 25.31(a), this petition qualifies for a categorical exemption from the requirement to submit an environmental assessment.

**D. Economic Impact Statement**

According to 21 C.F.R. § 10.30(b), petitioner will, upon request by the Commissioner, submit economic impact information.

**E. Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,



Robert W. Pollock  
Senior Vice President  
Lachman Consultant Services, Inc.  
1600 Stewart Avenue  
Westbury, NY 11590

RWP/bh

Attachment A:

Approved Drug Products with Therapeutic Equivalence Evaluations  
(Electronic Orange Book), Accessed September 30, 2005

Attachment B: Approved insert labeling for Didrex<sup>®</sup>

(Benzphetamine Hydrochloride Tablets, 50 mg)

Attachment C: Proposed insert labeling for Benzphetamine Hydrochloride Capsules, 50 mg

cc: Arianne Camphire (Office of Generic Drugs)

M24P5273

**LACHMAN CONSULTANT SERVICES, INC.**  
Westbury, NY 11590

**ATTACHMENT A**

## Proprietary Name Search Results from "OB\_Rx" table for query on "didrex."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
<u>012427</u>		Yes	BENZPHETAMINE HYDROCHLORIDE	TABLET; ORAL	50MG	DIDREX	PHARMACIA AND UPJOHN

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[Return to Electronic Orange Book Home Page](#)

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FDA/Center for Drug Evaluation and Research

Office of Generic Drugs

Division of Labeling and Program Support

Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through August, 2005

Patent and Generic Drug Product Data Last Updated: September 29, 2005

Search results from the "OB\_Rx" table for query on "012427."

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Active Ingredient: BENZPHETAMINE HYDROCHLORIDE  
Dosage Form;Route: TABLET; ORAL  
Proprietary Name: DIDREX  
Applicant: PHARMACIA AND UPJOHN  
Strength: 50MG  
Application Number: 012427  
Product Number: 002  
Approval Date: Approved Prior to Jan 1, 1982  
Reference Listed Drug: Yes  
RX/OTC/DISCN: RX  
TE Code:  
Patent and Exclusivity Info for this product: [View](#)

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**LACHMAN CONSULTANT SERVICES, INC.**  
Westbury, NY 11590

**ATTACHMENT B**

**Didrex®**  
benzphetamine  
hydrochloride tablets



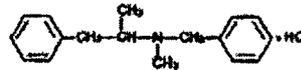
**PARKE-DAVIS**

**Didrex**  
brand of benzphetamine  
hydrochloride tablets

#### DESCRIPTION

DIDREX Tablets contain the anorectic agent benzphetamine hydrochloride. Benzphetamine hydrochloride is a white crystalline powder readily soluble in water and 95% ethanol. The chemical name for benzphetamine hydrochloride is  $\alpha$ -N, $\alpha$ -Dimethyl-N-(1-phenylmethyl)-benzeneethanamine hydrochloride and its molecular weight is 275.82.

The structural formula (dextro form) is represented below:



Each DIDREX Tablet, for oral administration, contains 50 mg of benzphetamine hydrochloride.

Inactive ingredients: Calcium Stearate, Corn Starch, Erythrosine Sodium, FD & C Yellow No. 6, Lactose, Povidone, Sorbitol.

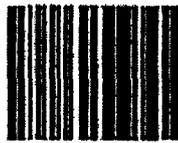
#### CLINICAL PHARMACOLOGY

Benzphetamine hydrochloride 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, 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.

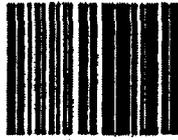
Adult obese subjects instructed in dietary management and treated with "anorectic" drugs, lose more weight on the average than those treated with

Didrex  
Tablets



0810735916

Didrex  
Tablets



0810735916

## **Didrex**

brand of benzphetamine  
hydrochloride tablets

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 the 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 drug 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 to be clinically limited.

Pharmacokinetic data in humans are not available.

### **INDICATIONS AND USAGE**

DIDREX Tablets are indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class (see CLINICAL PHARMACOLOGY) should be weighed against possible risks inherent in their use such as those described below.

### **CONTRAINDICATIONS**

DIDREX Tablets are contraindicated in patients with advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension,

## **Didrex**

brand of benzphetamine  
hydrochloride tablets

hyperthyroidism, known hypersensitivity or idiosyncrasy to sympathomimetic amines, and glaucoma. Benzphetamine should not be given to patients who are in an agitated state or who have a history of drug abuse.

Hypertensive crises have resulted when sympathomimetic amines have been used concomitantly or within 14 days following use of monoamine oxidase inhibitors. DIDREX should not be used concomitantly with other CNS stimulants.

DIDREX may cause fetal harm when administered to a pregnant woman. Amphetamines have been shown to be teratogenic and embryotoxic in mammals at high multiples of the human dose. DIDREX is contraindicated in women who are or may become pregnant. 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 the fetus.

### **WARNINGS**

When 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.

### **PRECAUTIONS**

General: Insulin requirements in diabetes mellitus may be altered in association with use of anorexigenic drugs and the concomitant dietary restrictions.

Psychological disturbances have been reported in patients who receive an anorectic agent together with a restrictive dietary regime.

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

## Didrex

brand of benzphetamine  
hydrochloride tablets

**Information for Patients:** Amphetamines 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.

**Drug Interactions:** Hypertensive crises have resulted when sympathomimetic amines have been used concomitantly or within 14 days following use of monoamine oxidase inhibitors. DIDREX should not be used concomitantly with other CNS stimulants.

Amphetamines may decrease the hypotensive effect of antihypertensives. Amphetamines may enhance the effects of tricyclic antidepressants.

Urinary alkalinizing agents increase blood levels and decrease excretion of amphetamines. Urinary acidifying agents decrease blood levels and increase excretion of amphetamines.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Animal studies to evaluate the potential for carcinogenesis, mutagenesis or impairment of fertility have not been performed by Pharmacia & Upjohn Company.

**Pregnancy:** Pregnancy Category X (see CONTRAINDICATIONS section).

**Nursing Mothers:** Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.

**Pediatric Use:** Use of benzphetamine hydrochloride is not recommended in individuals under 12 years of age.

**Geriatric Use:** Clinical studies of DIDREX Tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for

## Didrex

brand of benzphetamine  
hydrochloride tablets

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.

### ADVERSE REACTIONS

The following have been associated with the use of benzphetamine hydrochloride:

#### *Cardiovascular*

Palpitation, tachycardia, elevation of blood pressure. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

#### *CNS*

Overstimulation, restlessness, dizziness, insomnia, tremor, sweating, headache; rarely, psychotic episodes at recommended doses; depression following withdrawal of the drug.

#### *Gastrointestinal*

Dryness of the mouth, unpleasant taste, nausea, diarrhea, other gastrointestinal disturbances.

#### *Allergic*

Urticaria and other allergic reactions involving the skin.

#### *Endocrine*

Changes in libido.

### DRUG ABUSE AND DEPENDENCE

Benzphetamine is a controlled substance under the Controlled Substance Act by the Drug Enforcement Administration and has been assigned to Schedule III.

Benzphetamine hydrochloride is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of DIDREX Tablets 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

**Didrex**  
brand of benzphetamine  
hydrochloride tablets

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 intoxication is psychosis, often clinically indistinguishable from schizophrenia.

**OVERDOSAGE**

**Manifestations of Overdosage:** Acute overdose with amphetamines may result in restlessness, tremor, tachypnea, confusion, assaultiveness and 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. Hyperpyrexia and rhabdomyolysis have been reported and can lead to a number of associated complications. Fatal poisoning is usually preceded by convulsions and coma.

**Treatment of Overdosage:** (See WARNINGS)—Information concerning the effects of overdose with DIDREX Tablets is extremely limited. The following is based on experience with other anorexiant.

Management of acute amphetamine intoxication is largely symptomatic and includes sedation with a barbiturate. If hypertension is marked, the use of a nitrite or rapidly acting alpha receptor blocking agent should be considered.

**Didrex**  
brand of benzphetamine  
hydrochloride tablets

Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

Acidification of the urine increases amphetamine excretion.

The oral LD<sub>50</sub> is 174 mg/kg in mice and 104 mg/kg in rats. The intraperitoneal LD<sub>50</sub> in mice is 153 mg/kg.

**DOSAGE AND ADMINISTRATION**

Dosage should be individualized according to the response of the patient. The suggested dosage ranges from 25 to 50 mg one to three times daily. Treatment should begin with 25 to 50 mg once daily with subsequent increase in individual dose or frequency according to response. A single daily dose is preferably given in mid-morning or mid-afternoon, according to the patient's eating habits. In an occasional patient it may be desirable to avoid late afternoon administration. Use of benzphetamine hydrochloride is not recommended in individuals under 12 years of age.

**HOW SUPPLIED**

DIDREX Tablets are supplied as follows:  
50 mg (peach, round, imprinted with DIDREX 50, scored)  
Bottles of 100 NDC 0009-0024-01  
Bottles of 500 NDC 0009-0024-02  
Store at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

**Rx only**

Manufactured for:  
Pharmacia & Upjohn Company  
A subsidiary of Pharmacia Corporation  
Kalamazoo, Michigan 49001, USA

By: MOVA Pharmaceuticals  
Manati, PR 00674

Revised October 2003 810 735 916  
692167

**LACHMAN CONSULTANT SERVICES, INC.**  
Westbury, NY 11590

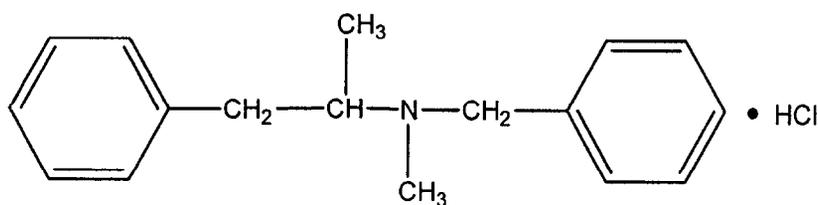
**ATTACHMENT C**

## Benzphetamine Hydrochloride Capsules

### DESCRIPTION

Benzphetamine hydrochloride capsules contain the anorectic agent benzphetamine hydrochloride. Benzphetamine hydrochloride is a white crystalline powder readily soluble in water and 95% ethanol. The chemical name for benzphetamine hydrochloride is *d*-N,  $\alpha$ -Dimethyl-N-(phenylmethyl) benzeneethanamine hydrochloride and its molecular weight is 275.82.

The structural formula (dextro form) is represented below:



Each benzphetamine hydrochloride capsule, for oral administration, contains 50 mg of benzphetamine hydrochloride.

Inactive ingredients: to be determined.

### CLINICAL PHARMACOLOGY

Benzphetamine hydrochloride 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, 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 is only a fraction of a pound a week. The rate of weight loss is the 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 drug 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 to be clinically limited.

Pharmacokinetic data in humans are not available.

#### **INDICATIONS AND USAGE**

Benzphetamine Hydrochloride Capsules are indicated in the management of exogenous obesity as a short term adjunct {a few weeks} in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of class {see CLINICAL PHARMACOLOGY} should be weighed against possible risks inherent in their use such as those described below.

#### **CONTRAINDICATIONS**

Benzphetamine Hydrochloride Capsules are contraindicated in [patients with advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to sympathomimetic amines, and glaucoma. Benzphetamine should not be given to patients who are in an agitated state or who have a history of drug abuse.

Hypertensive crises have resulted when sympathomimetic amines have been used concomitantly or within 14 days following use of monoamine oxidase inhibitors. Benzphetamine Hydrochloride Capsules should not be used concomitantly with other CNS stimulants.

Benzphetamine Hydrochloride Capsules may cause fetal harm when administered to a pregnant woman. Amphetamines have been shown to be teratogenic and embryotoxic in mammals at high multiples of the human dose. Benzphetamine Hydrochloride Capsules are contraindicated in women who are or may become pregnant. 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 the fetus.

#### **WARNINGS**

When 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.

## **PRECAUTIONS**

General: Insulin requirements in diabetes mellitus may be altered in association with use of anorexigenic drugs and the concomitant dietary restrictions.

Psychological disturbances have been reported in patients who receive an anorectic agent together with a restrictive dietary regime.

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

### **Information for patients:**

Amphetamines 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.

### **Drug Interaction:**

Hypertensive crisis have resulted when sympathomimetic amines have been used concomitantly or within 14 days following use of monoamine oxidase inhibitors. Benzphetamine Hydrochloride Capsules should not be used concomitantly with other CNS stimulants. Amphetamines may decrease the hypotensive effect of antihypertensives. Amphetamines may enhance the effects of tricyclic antidepressants. Urinary alkalinizing agents increase blood levels and decrease excretion of amphetamines. Urinary acidifying agents decrease blood levels and increase excretion of amphetamines.

### **Carcinogenesis, Mutagenesis, Impairment of Fertility:**

Animal studies to evaluate the potential for carcinogenesis, mutagenesis or impairment of fertility have not been performed by Pharmacia & Upjohn Company.

### **Pregnancy:**

Pregnancy Category X (see Contradictions section).

### **Nursing Mothers:**

Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.

### **Pediatric Use:**

Use of benzphetamine hydrochloride is not recommended in individuals under 12 years of age.

### **Geriatric Use:**

Clinical studies of Benzphetamine Hydrochloride Capsules did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in

responses between the elderly and younger patients. 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.

**Adverse Reactions:**

The following have been associated with the use of benzphetamine hydrochloride:

*Cardiovascular*

Palpitation, tachycardia, elevation of blood pressure. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

*CNS*

Overstimulation, restlessness, dizziness, insomnia, tremor, sweating, headache; rarely, psychotic episodes at recommended doses; depression following withdrawal of the drug.

*Gastrointestinal*

Dryness of the mouth, unpleasant taste, nausea, diarrhea, other gastrointestinal disturbances.

*Allergic*

Urticaria and other allergic reactions involving the skin

*Endocrine*

Changes in libido.

**Drug Abuse and Dependence**

Benzphetamine is a controlled substance under the Controlled Substance Act by the Drug Enforcement Administration and has been assigned to Schedule III.

Benzphetamine hydrochloride is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of Benzphetamine Hydrochloride Capsules 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 intoxication is psychosis, often clinically indistinguishable from schizophrenia.

**Overdosage**

**Manifestations of Overdosage:**

Acute overdosage with amphetamines may result in restlessness, tremor, tachypnea, confusion, assaultiveness and 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. Hyperpyrexia and rhabdomyolysis have been

reported and can lead to a number of associated complications. Fatal poisoning is usually preceded by convulsions and coma.

**Treatment of Overdosage:**

(See WARNINGS)- Information concerning the effects of overdosage with Benzphetamine Hydrochloride Capsules is extremely limited. The following is based on experience with other anorexiant.

Management of acute amphetamine intoxications largely symptomatic and includes sedation with a barbiturate. If hypertension is marked, the use of a nitrite or rapidly acting alpha receptor blocking agent should be considered.

Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard. Acidification of the urine increases amphetamine excretion. The oral LD<sub>50</sub> is 174 mg/kg in mice and 104 mg/kg in rats. The intraperitoneal LD<sub>50</sub> in mice is 153 mg/kg.

**Dosage and Administration**

Dosage should be individualized according to the response of the patient. The suggested dosage ranges from 25 to 50 mg one to three times daily. Treatment should begin with 25 to 50 mg once daily with subsequent increase in individual dose or frequency according to response. A single daily dose is preferably given in mid-morning or mid-afternoon, according to the patient's it may be desirable to avoid late afternoon administration. Use of benzphetamine hydrochloride is not recommended in individuals under 12 years of age.

**How Supplied**

Benzphetamine Hydrochloride Capsules are supplied as follows:

50 mg, NDC 0000-0000-00

Dosage Form: Capsule

Shape, Color, and Scoring: To be determined.

Packaging: To be determined

**Storage:** Store at controlled room temperature 20° to 25°C (68° to 77°F) [see USP]

Manufactured by:

Manufacturer

Code: 000000

Rev. 09/2005