

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

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July 15, 2004

OVERNIGHT COURIER 7/15/04

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

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act, and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Benzonatate Capsules USP, 150 mg, is suitable for consideration in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Benzonatate Capsules USP, 150 mg, are suitable for submission as an ANDA. The reference-listed drug product (RLD), upon which this petition is based, is Tessalon® Capsules (benzonatate), 200 mg by Forest Laboratories, Inc. The petitioner also references Tessalon® Capsules 100 mg, in support of this petition. Therefore, the petitioner seeks a change in strength (from 200 mg to 150 mg), from that of the listed drug product.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a drug product that differs in dosage strength from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Tessalon® Capsules by Forest Laboratories, Inc. is a capsule product containing 200 mg of benzonatate. See listing on page 3-45 of the 24th Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations* (Attachment 1). The proposed drug product also represents a capsule dosage form, but containing 150 mg of benzonatate. The petition is thus seeking a change in strength (from 200 mg to 150 mg), from that of the RLD. Please note that the proposed change in strength represents a dosage strength midway between the two currently approved 100 mg and 200 mg strengths of benzonatate.

The acceptability of the proposed 150 mg strength is contemplated in the labeling of the listed drug. The current dosing instructions in the approved labeling of the RLD are as follows:

"Adults and children over 10: Usual dose is one 100 mg or 200 mg capsule t.i.d. as required. If necessary, up to 600 mg daily may be given."

2004P-0321

CP 1

A 150 mg capsule would permit administration of an intermediate dose for those patients who may require greater than 100 mg, but less than 200 mg for relief of symptoms. Because this drug product is not without the potential for significant adverse reactions, the intermediate strength product would also give the health care practitioner greater flexibility in selecting the most appropriate dose for the patient while minimizing potential adverse events.

There are no proposed changes in labeling with the exception of the obvious changes in strength sought in this petition. The uses, indications, warnings and directions for use will remain the same as that of the RLD. Draft labeling for the proposed product is included in Attachment 2, and the RLD's approved labeling is provided in Attachment 3.

Therefore, the petitioner's request for the Commissioner to find that a change in strength from 200 mg to 150 mg, for Benzonatate Capsules USP should raise no questions of safety or effectiveness, and the Agency should approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis if requested by the Agency.

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
Vice President
Lachman Consultant Services, Inc.
1600 Stewart Avenue
Westbury, NY 11590

RWP/pk

- Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, 24th Edition, Page 3-45
 2. Draft Insert Labeling Proposed for Benzonatate Capsules
 3. Labeling for Tessalon®

cc: Emily Thakur (OGD)

A43P4197

LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

ATTACHMENT 1

PRESCRIPTION DRUG PRODUCT LIST

BENAZEPRIL HYDROCHLORIDE; HYDROCHLOROTHIAZIDE

TABLET; ORAL LOTENSIN HCT NOVARTIS	5MG; 6.25MG	N20033 001 MAY 19, 1992
	10MG; 12.5MG	N20033 002 MAY 19, 1992
	20MG; 12.5MG	N20033 004 MAY 19, 1992
+	20MG; 25MG	N20033 003 MAY 19, 1992

BENDROFLUMETHIAZIDE

TABLET; ORAL NATURETIN-5 + APOTHECON	5MG	N12164 002
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BENDROFLUMETHIAZIDE; NADOLOL

TABLET; ORAL CORZIDE KING PHARMS	5MG; 40MG	N18647 001 MAY 25, 1983
+	5MG; 80MG	N18647 002 MAY 25, 1983

BENZONATATE

CAPSULE; ORAL <u>BENZONATATE</u> AA BANNER PHARMACAPS	<u>100MG</u>	N81297 001 JAN 29, 1993
AA + <u>TESSALON</u> FOREST LABS	<u>100MG</u>	N11210 001
+	200MG	N11210 003 JUN 25, 1999

BENZOYL PEROXIDE; CLINDAMYCIN PHOSPHATE

GEL; TOPICAL BENZAACLIN + DERMIK LABS	5%; EQ 1% BASE	N50756 001 DEC 21, 2000
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BENZOYL PEROXIDE; CLINDAMYCIN P

GEL; TOPICAL DUAC + STIEFEL	5%; E
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BENZOYL PEROXIDE; ERYTHROMYCIN

GEL; TOPICAL BENZAMYCIN + DERMIK LABS	5%; 3
BENZAMYCIN PAK + DERMIK LABS	5%; 3

BENZPHETAMINE HYDROCHLORIDE

TABLET; ORAL DIDREX + PHARMACIA AND UPJOHN	50MG
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BENZQUINAMIDE HYDROCHLORIDE

INJECTABLE; INJECTION EMETE-CON + PFIZER	EQ 5
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BENZTROPINE MESYLATE

INJECTABLE; INJECTION COGENTIN + MERCK	1MG/1
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TABLET; ORAL <u>BENZTROPINE MESYLATE</u> AA COREPHARMA	<u>0.5M</u>
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AA	<u>1MG</u>
AA	<u>2MG</u>
AA	<u>1MG</u>

AA	MUTUAL PHARM	<u>1MG</u>
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LACHMAN CONSULTANT SERVICES, INC.
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ATTACHMENT 2

PRECAUTIONS

Benzonatate is chemically related to anesthetic agents of the para-amino-benzoic acid class (e.g., procaine; tetracaine) and has been associated with adverse CNS effects possibly related to a prior sensitivity to related agents or interaction with concomitant medication.

Information for Patients: Release of benzonatate from the capsule in the mouth can produce a temporary local anesthesia of the oral mucosa and choking could occur. Therefore, the capsules should be swallowed without chewing.

Usage in Pregnancy: Pregnancy Category C. Animal reproduction studies have not been conducted with benzonatate. It is also not known whether benzonatate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Benzonatate should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk caution should be exercised when benzonatate is administered to a nursing woman.

Carcinogenesis, Mutagenesis, Impairment of Fertility : Carcinogenicity, mutagenicity, and reproduction studies have not been conducted with benzonatate.

Pediatric Use: Safety and effectiveness in children below the age of 10 has not been established.

ADVERSE REACTIONS

Potential Adverse Reactions to benzonatate may include:

Hypersensitivity reactions including bronchospasm, laryngospasm, cardiovascular collapse possibly related to local anesthesia from chewing or sucking the capsule.

CNS: sedation; headache; dizziness; mental confusion; visual hallucinations.

GI: constipation, nausea, GI upset.

Dermatologic: pruritus; skin eruptions.

Other: nasal congestion; sensation of burning in the eyes; vague "chilly" sensation; numbness of the chest; hypersensitivity.

Rare instances of deliberate or accidental overdose have resulted in death.

OVERDOSAGE

Overdose may result in death.

The drug is chemically related to tetracaine and other topical anesthetics and shares various aspects of their pharmacology and toxicology. Drugs of this type are generally well absorbed after ingestion.

Signs and Symptoms:

If capsules are chewed or dissolved in the mouth, oropharyngeal anesthesia will develop rapidly. CNS stimulation may cause restlessness and tremors which may proceed to clonic convulsions followed by profound CNS depression.

Treatment:

Evacuate gastric contents and administer copious amounts of activated charcoal slurry. Even in the conscious patient, cough and gag reflexes may be so depressed as to necessitate special attention to protection against aspiration of gastric contents and orally administered materials. Convulsions should be treated with a short-acting barbiturate given intravenously and carefully titrated for the smallest effective dosage. Intensive support of respiration and cardiovascular-renal function is an essential feature of the treatment of severe intoxication from overdose.

Do not use CNS stimulants.

DOSAGE AND ADMINISTRATION:

Adults and Children over 10: Usual dose is one 100 mg , 150 mg or 200mg capsule t.i.d. as required. If necessary, up to 600 mg daily may be given.

HOW SUPPLIED

Capsules, 100 mg bottles of 100
NDC 0000-0000-00 Imprint: XXXX

Capsules, 150 mg bottles of 100
NDC 0000-0000-00 Imprint: XXXX.

Capsules, 200 mg bottles of 100
NDC 0000-0000-00 Imprint: XXXX

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

Rev. XX/XX

Mfd by
XXXXXX
XXXXXXXX, XXXXXXXX XXXXX
for

XXXXXXXXXXXXXXXXXXXX

©2004 XXXXXXXXXXXXXXXXXXXX

Please note that information in the How Supplied section of the labeling will be completed at the time of submission of the ANDA.

LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

ATTACHMENT 3

PRECAUTIONS

Benzonatate is chemically related to anesthetic agents of the para-amino-benzoic acid class (e.g., procaine; tetracaine) and has been associated with adverse CNS effects possibly related to a prior sensitivity to related agents or interaction with concomitant medication.

Information for Patients: Release of TESSALON from the capsule in the mouth can produce a temporary local anesthesia of the oral mucosa and choking could occur. Therefore, the capsules should be swallowed without chewing.

Usage in Pregnancy: Pregnancy Category C. Animal reproduction studies have not been conducted with TESSALON. It is also not known whether TESSALON can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. TESSALON should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk caution should be exercised when TESSALON is administered to a nursing woman.

Carcinogenesis, Mutagenesis, Impairment of Fertility : Carcinogenicity, mutagenicity, and reproduction studies have not been conducted with TESSALON.

Pediatric Use: Safety and effectiveness in children below the age of 10 has not been established.

ADVERSE REACTIONS

Potential Adverse Reactions to TESSALON may include:

Hypersensitivity reactions including bronchospasm, laryngospasm, cardiovascular collapse possibly related to local anesthesia from chewing or sucking the capsule.

CNS: sedation; headache; dizziness; mental confusion; visual hallucinations.

GI: constipation, nausea, GI upset.

Dermatologic: pruritus; skin eruptions.

Other: nasal congestion; sensation of burning in the eyes; vague "chilly" sensation; numbness of the chest; hypersensitivity.

Rare instances of deliberate or accidental overdose have resulted in death.

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If capsules are chewed or dissolved in the mouth, oropharyngeal anesthesia will develop rapidly. CNS stimulation may cause restlessness and tremors which may proceed to clonic convulsions followed by profound CNS depression.

Treatment:

Evacuate gastric contents and administer copious amounts of activated charcoal slurry. Even in the conscious patient, cough and gag reflexes may be so depressed as to necessitate special attention to protection against aspiration of gastric contents and orally administered materials. Convulsions should be treated with a short-acting barbiturate given intravenously and carefully titrated for the smallest effective dosage. Intensive support of respiration and cardiovascular-renal function is an essential feature of the treatment of severe intoxication from overdosage.

Do not use CNS stimulants.

DOSAGE AND ADMINISTRATION:

Adults and Children over 10: Usual dose is one 100 mg or 200 mg capsule t.i.d. as required. If necessary, up to 600 mg daily may be given.

HOW SUPPLIED

Perles, 100 mg (yellow); bottles of 100
NDC 0456-0688-01 Imprint: T.

Perles, 100 mg (yellow); bottles of 500
NDC 0456-0688-02 Imprint: T.

Capsules, 200 mg (yellow); bottles of 100
NDC 0456-0698-01 Imprint: 0698.

Capsules, 200 mg (yellow); bottles of 500
NDC 0456-0698-02 Imprint: 0698.

Store at 25 °C (77 °F); excursions permitted to 15-30 °C
(59-86 °F) [see USP Controlled Room Temperature].

Rev. 3/03 (04)

Mfd by
Cardinal Health
St. Petersburg, Florida 33716
for

FOREST PHARMACEUTICALS, INC.
SUBSIDIARY OF FOREST LABORATORIES, INC.
ST. LOUIS, MISSOURI 63045
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