

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 074795

**Trade Name :FLUPHENAZINE DECANOATE
INJECTION USP 25MG/ML**

Generic Name:Fluphenazine Decanoate Inj USP 25mg/ml

Sponsor : Gensia Laboratories, Inc.

Approval Date: September 10, 1996

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 074795 _____

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				
Approvable Letter				
Final Printed Labeling	X			
Medical Review(s)				
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)				
Statistical Review(s)				
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)				
Bioequivalence Review(s)	X			
Administrative Document(s)				
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 074795

APPROVAL LETTER

SEP 10 1996

Gensia Laboratories, Inc.
Attention: Donald J. Harrigan, R.Ph.
19 Hughes
Irvine, CA 92718-1902

Dear Sir:

This is in reference to your abbreviated new drug application dated November 30, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Fluphenazine Decanoate Injection USP, 25 mg/mL, packaged in 5 mL multiple-dose vials.

Reference is also made to your amendment dated August 1, 1996.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined that your Fluphenazine Decanoate Injection USP, 25 mg/mL is bioequivalent and, therefore, therapeutically equivalent to the listed drug (Prolixin Decanoate® Injection, 25 mg/mL, of Apothecon, Inc.).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaign. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign, at the time of their initial use, be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253.

Sincerely yours,

[Redacted] /S/ [Redacted] 8/10/96

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 74-795
ANANDA 74-795/Division File
Field Copy
HFD-600/Reading File
HFD-82
HFD-8/PSavino
HFD-110/JPhillips

Endorsement:

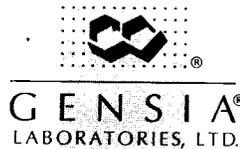
HFD-627/NNashed/8-26-96
HFD-613/J.Grace for Ave
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HFD-620/KMuhvich/8-26-9
HFD-627/PSchwartz, PhD/
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F/T by MM August 27, 19
APPROVAL LETTER

[Redacted] /S/ [Redacted] 4/10/96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 074795

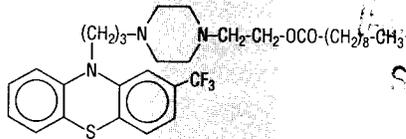
FINAL PRINTED LABELING



Fluphenazine Decanoate Injection, USP

DESCRIPTION:

Fluphenazine decanoate is the decanoate ester of a trifluoromethyl phenothiazine derivative. Fluphenazine Decanoate is 2-4-[3-(2-trifluoromethylphenothiazin-10-yl)-propyl]-piperazin-1-ylethyl deconoate. It is a highly potent behavior modifier with a markedly extended duration of effect and has the following structural formula:



$C_{32}H_{44}F_3N_3O_2S$

591.8

Fluphenazine Decanoate Injection, USP is a sterile solution available for intramuscular (IM) or subcutaneous (SC) use providing 25 mg fluphenazine decanoate per mL in a sesame oil vehicle with 12 mg benzyl alcohol as a preservative.

CLINICAL PHARMACOLOGY:

The basic effects of fluphenazine decanoate appear to be no different from those of fluphenazine hydrochloride, with the exception of duration of action. The esterification of fluphenazine markedly prolongs the drug's duration of effect without unduly attenuating its beneficial action.

Fluphenazine decanoate has activity at all levels of the central nervous system (CNS) as well as on multiple organ systems. The mechanism whereby its therapeutic action is exerted is unknown.

Fluphenazine differs from other phenothiazine derivatives in several respects: it is more potent on a milligram basis, it has less potentiating effect on CNS depressants and anesthetics than do some of the phenothiazines and appears to be less sedating, and it is less likely than some of the older phenothiazines to produce hypotension (nevertheless, appropriate cautions should be observed - see PRECAUTIONS and ADVERSE REACTIONS)

INDICATIONS AND USAGE:

Fluphenazine Decanoate Injection is a long-acting parenteral antipsychotic drug intended for use in the management of patients requiring prolonged parenteral neuroleptic therapy (e.g., chronic schizophrenics).

Fluphenazine Decanoate Injection has not been shown effective in the management of behavioral complications in patients with mental retardation.

CONTRAINDICATIONS:

Phenothiazines are contraindicated in patients with suspected or established subcortical brain damage.

Phenothiazine compounds should not be used in patients receiving large doses of hypnotics.

Fluphenazine Decanoate Injection is contraindicated in comatose or severely depressed states.

The presence of blood dyscrasia or liver damage precludes the use of fluphenazine decanoate.

Fluphenazine Decanoate Injection is not intended for use in children under 12 years of age. Fluphenazine Decanoate Injection is contraindicated in patients who have shown hypersensitivity to fluphenazine: cross-sensitivity to phenothiazine derivatives may occur.

WARNINGS:

Tardive Dyskinesia

Tardive dyskinesia, a syndrome consisting of potential irreversible, involuntary, dyskinetic movements, may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn.

Neuroleptic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, neuroleptics should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to neuroleptic drugs, and, 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

(For further information about the description of tardive dyskinesia and its clinical detection, please refer to the sections on PRECAUTIONS, Information for Patients, and ADVERSE REACTIONS, Tardive Dyskinesia.)

Neuroleptic Malignant Syndrome (NMS)

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias).

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary CNS pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

The use of this drug may impair the mental and physical abilities required for driving a car or operating heavy machinery.

Physicians should be alert to the possibility that severe adverse reactions may occur which require immediate medical attention.

Potential of the effects of alcohol may occur with the use of this drug.

Since there is no adequate experience in children who have received this drug, safety and efficacy in children have not been established.

Pregnancy

The safety for the use of this drug during pregnancy has not been established; therefore, the possible hazards should be weighed against the potential benefits when administering this drug to pregnant patients.

PRECAUTIONS:

General

Because of the possibility of cross-sensitivity, fluphenazine decanoate should be used cautiously in patients who have developed cholestatic jaundice, dermatoses, or other allergic reactions to phenothiazine derivatives.

Psychotic patients on large doses of a phenothiazine drug who are undergoing surgery should be watched carefully for possible hypotensive phenomena. Moreover, it should be remembered that reduced amounts of anesthetics or CNS depressants may be necessary.

The effects of atropine may be potentiated in some patients receiving fluphenazine because of added anticholinergic effects.

Fluphenazine decanoate should be used cautiously in patients exposed to extreme heat or phosphorus insecticides.

The preparation should be used with caution in patients with a history of convulsive disorders, since grand mal convulsions have been known to occur.

Use with caution in patients with special medical disorders such as mitral insufficiency or other cardiovascular disease and pheochromocytoma.

The possibility of liver damage, pigmentary retinopathy, lenticular and corneal deposits, and development of irreversible dyskinesia should be remembered when patients are on prolonged therapy.

Outside state hospitals or other psychiatric institutions, fluphenazine decanoate should be administered under the direction of a physician experienced in the clinical use of psychotropic drugs, particularly phenothiazine derivatives. Furthermore, facilities should be available for periodic checking of hepatic function, renal function, and the blood picture. Renal function of patients on long-term therapy should be monitored; if blood urea nitrogen (BUN) becomes abnormal, treatment should be discontinued.

As with any phenothiazine, the physician should be alert to the possible development of "silent pneumonias" in patients under treatment with fluphenazine decanoate.

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Information for Patients

Given the likelihood that some patients exposed chronically to neuroleptics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided.

ADVERSE REACTIONS:

Central Nervous System

The side effects most frequently reported with phenothiazine compounds are extrapyramidal symptoms including pseudoparkinsonism, dystonia, dyskinesia, akathisia, oculogyric crises, opisthotonos, and hyperreflexia. Muscle rigidity sometimes accompanied by hyperthermia has been reported following use of fluphenazine decanoate. Most often these extrapyramidal symptoms are reversible; however, they may be persistent (see below). The frequency of such reactions is related in part to chemical structure: one can expect a higher incidence with fluphenazine decanoate than with less potent piperazine derivatives or with straight-chain phenothiazines such as chlorpromazine. With any given phenothiazine derivative, the incidence and severity of such reactions depend more on individual patient sensitivity than on other factors, but dosage level and patient age are also determinants.

Extrapyramidal reactions may be alarming, and the patient should be forewarned and reassured. These reactions can usually be controlled by administration of antiparkinsonian drugs such as Benztropine Mesylate or intravenous Caffeine and Sodium Benzoate Injection, and by subsequent reduction in dosage.

Tardive Dyskinesia

See **WARNINGS**. The syndrome is characterized by involuntary choreoathetoid movements which variously involve the tongue, face, mouth, lips, or jaw (e.g., protrusion of the tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk and extremities. The severity of the syndrome and the degree of impairment produced vary widely.

The syndrome may become clinically recognizable either during treatment, upon dosage reduction, or upon withdrawal of treatment. Early detection of tardive dyskinesia is important. To increase the likelihood of detecting the syndrome at the earliest possible time, the dosage of the neuroleptic drug should be reduced periodically (if clinically possible) and the patient observed for signs of the disorder. This maneuver is critical, since neuroleptic drugs may mask the signs of the syndrome.

Other CNS Effects

Occurrences of neuroleptic malignant syndrome (NMS) have been reported in patients on neuroleptic therapy (see **WARNINGS**, Neuroleptic Malignant Syndrome); leukocytosis, elevated CPK, liver function abnormalities, and acute renal failure may also occur with NMS. Drowsiness or lethargy, if they occur, may necessitate a reduction in dosage; the induction of a catatonic-like state has been known to occur with dosages of fluphenazine far in excess of the recommended amounts. As with other phenothiazine compounds, reactivation or aggravation of psychotic processes may be encountered.

Phenothiazine derivatives have been known to cause, in some patients, restlessness, excitement, or bizarre dreams.

Autonomic Nervous System

Hypertension and fluctuations in blood pressure have been reported with fluphenazine. Hypotension has rarely presented a problem with fluphenazine. However, patients with pheochromocytoma, cerebral, vascular or renal insufficiency, or a severe cardiac reserve deficiency such as mitral insufficiency appear to be particularly prone to hypotensive reactions with phenothiazine compounds, and should therefore be observed closely when the drug is administered. If severe hypotension should occur, supportive measures including the use of intravenous vasopressor drugs should be instituted immediately. Levarterenol Bitartrate Injection is the most suitable drug for this purpose; epinephrine should not be used since phenothiazine derivatives have been found to reverse its action, resulting in a further lowering of blood pressure.

Autonomic reactions including nausea and loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, and constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily discontinuing dosage.

In some patients, phenothiazine derivatives have caused blurred vision, glaucoma, bladder paralysis, fecal impaction, paralytic ileus, tachycardia, or nasal congestion.

Metabolic and Endocrine

Weight change, peripheral edema, abnormal lactation, gynecomastia, menstrual irregularities, false results on pregnancy tests, impotency in men and increased libido in women have all been known to occur in some patients on phenothiazine therapy.

Allergic Reactions

Skin disorders such as itching, erythema, urticaria, seborrhea, photosensitivity, eczema and even exfoliative dermatitis have been reported with phenothiazine derivatives. The possibility of anaphylactoid reactions occurring in some patients should be borne in mind.

Hematologic

Routine blood counts are advisable during therapy since blood dyscrasias including leukopenia, agranulocytosis, thrombocytopenic or nonthrombocytopenic purpura, eosinophilia, and pancytopenia have been observed with phenothiazine derivatives. Furthermore, if any soreness of the mouth, gums, or throat, or any symptoms of upper respiratory infection occur and confirmatory leukocyte count indicates cellular depression, therapy should be discontinued and other appropriate measures instituted immediately.

Hepatic

Liver damage as manifested by cholestatic jaundice may be encountered, particularly during the first months of therapy; treatment should be discontinued if this occurs. An increase in cephalin flocculation, sometimes accompanied by alterations in other liver function tests, has been reported in patients receiving the enanthate ester of fluphenazine (a closely related compound) who have had no clinical evidence of liver damage.

Others

Sudden, unexpected and unexplained deaths have been reported in hospitalized psychotic patients receiving phenothiazines. Previous brain damage or seizures may be predisposing factors; high doses should be avoided in known seizure patients. Several patients have shown sudden flare-ups of psychotic behavior patterns shortly before death. Autopsy findings have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric contents, or intramyocardial lesions.

Although this is not a general feature of fluphenazine, potentiation of CNS depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) may occur.

The following adverse reactions have also occurred with phenothiazine derivatives: systemic lupus erythematosus-like syndrome, hypotension severe enough to cause fatal cardiac arrest, altered electrocardiographic and electroencephalographic tracings, altered cerebrospinal fluid proteins, cerebral edema, asthma, laryngeal edema, and angioneurotic edema; with long-term use - skin pigmentation, and lenticular and corneal opacities.

Injections of fluphenazine decanoate are extremely well tolerated, local tissue reactions occurring only rarely.

DOSAGE AND ADMINISTRATION:

Fluphenazine Decanoate Injection may be given IM or SC. A dry syringe and needle of at least 21 gauge should be used. Use of a wet needle or syringe may cause the solution to become cloudy.

To begin therapy with Fluphenazine Decanoate Injection the following regimens are suggested:

For most patients, a dose of 12.5 to 25 mg (0.5 to 1 mL) may be given to initiate therapy. The onset of action generally appears between 24 and 72 hours after injection and the effects of the drug on psychotic symptoms become significant within 48 to 96 hours. Subsequent injections and the dosage interval are determined in accordance with the patient's response. When administered as maintenance therapy, a single injection may be effective in controlling schizophrenic symptoms up to four weeks or longer. The response to a single dose has been found to last as long as six weeks in a few patients on maintenance therapy.

It may be advisable that patients who have no history of taking phenothiazines should be treated initially with a shorter-acting form of fluphenazine before administering the decanoate to determine the patient's response to fluphenazine and to establish appropriate dosage. For psychotic patients who have been stabilized on a fixed daily dosage of Fluphenazine Hydrochloride Tablets or Fluphenazine Hydrochloride Elixir, or Fluphenazine Hydrochloride Oral Solution conversion of therapy from these short-acting oral forms to the long-acting Fluphenazine Decanoate Injection may be indicated.

Appropriate dosage of Fluphenazine Decanoate Injection should be individualized for each patient and responses carefully monitored. No precise formula can be given to convert to use of Fluphenazine Decanoate Injection; however, a controlled multicentered study*, in patients receiving oral doses from 5 to 60 mg fluphenazine hydrochloride daily, showed that 20 mg fluphenazine hydrochloride daily was equivalent to 25 mg (1 mL) of Fluphenazine Decanoate Injection every three weeks. This represents an approximate conversion ratio of 12.5 mg (0.5 mL) of decanoate every three weeks for every 10 mg of fluphenazine hydrochloride daily.

Once conversion to Fluphenazine Decanoate Injection is made, careful clinical monitoring of the patient and appropriate dosage adjustment should be made at the time of each injection.

Severely agitated patients may be treated initially with a rapid-acting phenothiazine compound such as Fluphenazine Hydrochloride Injection -see package insert accompanying that product for complete information. When acute symptoms have subsided, 25 mg (1 mL) of Fluphenazine Decanoate Injection may be administered; subsequent dosage is adjusted as necessary.

"Poor risk" patients (those with known hypersensitivity to phenothiazines, or with disorders that predispose to undue reactions): Therapy may be initiated cautiously with oral or parenteral fluphenazine hydrochloride (see package inserts accompanying these products for complete information). When the pharmacologic effects and an appropriate dosage are apparent, an equivalent dose of Fluphenazine Decanoate Injection may be administered. Subsequent dosage adjustments are made in accordance with the response of the patient.

The optimal amount of the drug and the frequency of administration must be determined for each patient, since dosage requirements have been found to vary with clinical circumstances as well as with individual response to the drug.

Dosage should not exceed 100 mg. If doses greater than 50 mg are deemed necessary, the next dose and succeeding doses should be increased cautiously in increments of 12.5 mg.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

Fluphenazine Decanoate Injection, USP 125 mg/5 mL (25 mg/mL) is supplied as follows:

NDC Number	SIZE
N0703-5003-01	5 mL Vial

5 mL Multiple Dose Vials are packaged individually.

Store at controlled room temperature 15° to 30°C (59° to 86°F). Avoid freezing and excessive heat.

PROTECT FROM LIGHT. Retain vial in carton until ready for use.

CAUTION: Federal (USA) law prohibits dispensing without prescription.

*Schooler, N.R.: The Initiation of Long-Term Pharmacotherapy in Schizophrenia: Dosage and Side Effect Comparisons between Oral and Depot Fluphenazine; Pharmacopsych. 9:159-169, 1976.

Issued: July 1996

Gensia Laboratories, Ltd.
Irvine CA 92718

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 074795

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 2
2. ANDA # 74-795
3. NAME AND ADDRESS OF APPLICANT
Gensia Laboratories, Ltd.
19 Hughes
Irvine, CA 92718
4. LEGAL BASIS FOR SUBMISSION
See Chemist's Review #1
5. SUPPLEMENT(s) N/A
6. PROPRIETARY NAME N/A
7. NONPROPRIETARY NAME Fluphenazine Decanoate
8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A
9. AMENDMENTS AND OTHER DATES:
Original 11/30/95
Amendment 1/4/96
Amendment 8/1/96
10. PHARMACOLOGICAL CATEGORY Antipsychotic
11. Rx or OTC Rx
12. RELATED IND/NDA/DMF(s)
|(b)4 - Confidential|
13. DOSAGE FORM Liquid
14. POTENCY 25 mg/mL
15. CHEMICAL NAME AND STRUCTURE
2-4-[3-(2-trifluoromethylphenothiazin-10-yl)-propyl]-
piperazin-1-yl]ethyl decanoate
16. RECORDS AND REPORTS
17. COMMENTS
The microbiological portion is satisfactory 8/14/96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 074795

BIOEQUIVALENCE REVIEW(S)

ANDA 74-795

MAY - 6 1996

Gensia Laboratories, Ltd.
Attention: Donald J. Harrigan
19 Hughes
Irvine CA 92718-1902
|||||

Dear Sir:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Fluphenazine Decanoate Injection USP, 25 mg/ mL, 5 mL vials.

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,



Keith R. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

APR 29 1996

Fluphenazine Decanoate
Injection 25 mg/mL
ANDA #74-795
Reviewer A.P.Patel
File: x:\apatel\74795w.n95

Gensia Laboratories, Ltd.
Irvine, CA
Submission Date:
Nov. 30, 1995

Review of a Waiver Request

Introduction:

Fluphenazine Decanoate Injection is a long-acting parenteral antipsychotic drug intended for use in the management of patients requiring prolonged parenteral neuroleptic therapy.

Objective:

The firm is requesting a waiver of *in vivo* bioequivalence study requirements for its Fluphenazine Decanoate Injection, 25 mg/mL. The reference listed drug is Prolixin Decanoate[®] (Fluphenazine Decanoate Injection) 25 mg/mL, manufactured by Apothecon[®]. The drug is to be administered by intramuscular or subcutaneous injections.

Comments:

1. The test product is a parenteral solution intended solely for administration by injection.
2. The formulation of the test product contains the same active and inactive ingredients in the same concentration as the approved reference product Prolixin Decanoate^R Injection 25 mg/mL.
3. Comparative formulation: Please see Table 1.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Gensia Laboratories, Ltd., demonstrates that Fluphenazine Decanoate Injection, 25 mg/mL, falls under Section 320.22 (b)(1) of Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study for the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test injectable formulation manufactured by Gensia Laboratories, Ltd., to be bioequivalent to Prolixin Decanoate[®] (Fluphenazine Decanoate Injection) manufactured by Apothecon[®].

The firm should be informed of the above recommendation.



A.P. Patel
Division of Bioequivalence
Review Branch III

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Comparative formulation:

Table 1

Ingredients	Gensia's Formulation	Apothecon's Formulation
	Each mL contains	Each mL contains
Fluphenazine Decanoate, USP	25 mg	25 mg
Benzyl Alcohol, NF	12 mg	12 mg
Sesame Oil	q.s. to 1.0 mL	q.s. to 1.0 mL

NDC 0703-5003-01
Unit Carton
(Part No. X12-500-301)

25 mg/mL, 125 mg in a 5 mL Multiple Dose Vial

SEP 10 1996

APPROVED

Fluphenazine
Decanoate
Injection, USP
125 mg/5 mL
25 mg/mL

Gensia Laboratories, Ltd.
NDC 0703-5003-01

**Fluphenazine
Decanoate
Injection, USP**

**125 mg/5 mL
25 mg/mL**

For IM or SC Use

5 mL Multiple
Dose Vial

AVOID ERRORS, READ
CAREFULLY

Each contains:

Fluphenazine Decanoate,
USP 25 mg in sesame
oil; Benzyl Alcohol 12 mg
as a preservative.

• Sterile. • Dosage:
See Package Insert •
Store at controlled room
temperature to 30°C

(59° to 86° F).
Avoid freezing and exces-
sive heat.

PROTECT FROM LIGHT.

Retain vial in carton until

ready for use.

Caution: Federal (USA)
law prohibits dispensing
without prescription.

Gensia Laboratories, Ltd.
NDC 0703-5003-01

**Fluphenazine
Decanoate
Injection, USP**

**125 mg/5 mL
25 mg/mL**

For IM or SC Use

5 mL Multiple
Dose Vial

See bottom panel for Lot Number and Expiration Date.
Gensia Laboratories, Ltd.
Irvine CA 92718
X12-500-301

NDC 0703-5003-01
Container Label
(Part No. Y29-500-301)

25 mg/mL, 125 mg in a 5 mL Multiple Dose Vial

