CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 40-776

Name: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

Sponsor: Outlook Pharmaceuticals, Inc.

Approval Date: January 29, 2008

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 40-776

Outlook Pharmaceuticals, Inc.
U.S. Agent: Mikart, Inc.
Attention: Lisa Apolis
Manager, Regulatory Submissions
1750 Chattahoochee Avenue
Atlanta, GA 30318

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated April 28, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL.

Reference is also made to your amendments dated March 23, May 22, June 1, September 14, and November 14, 2007; and January 16, 2008.

We note that the reference listed drug product (RLD) upon which you have based this application, Dexedrine Oral Solution (Elixir) of GlaxoSmithKline (GSK), is no longer being marketed in the United States. Thus, GSK's Dexedrine Oral Solution was moved to the Discontinued section of the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book". Reference is made to the Federal Register Notice dated August 7, 2007 (Volume 72, No. 151) in which the agency announced its determination that Dexedrine Oral Solution (Elixir) was not withdrawn from sale for reasons of safety or effectiveness. This determination allows the agency to approve ANDAs for the discontinued drug product.

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. When used as recommended in the labeling, the drug product, Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL, can be expected to have the same

therapeutic effect as that of the former reference listed drug product upon which the agency relied as the basis of safety and effectiveness.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert L. West
1/29/2008 09:00:55 AM
for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

LABELING

NDC 46672-646-16

CII

DEXTROAMPHETAMINE SULFATE ORAL SOLUTION

5 mg/5 mL

Rx only

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

Dispense in a tight, light-resistant container.

WARNING: Keep this and all medications out of the reach of children.

3 46672 64616 1

Lot:

Exp.:

PHARMACIST:
Dispense Medication Guide with the Drug Product

16 fl. oz. (473 mL)

USUAL DOSAGE: See package insert for complete dosage recommendations.

WARNING: May be habit-forming.

Each 5 mL contains dextroamphetamine sulfate, 5 mg.

Manufactured by:
Mikart, Inc.
Atlanta, GA 30318

Code 983Z10 Rev. 10/07

PRESCRIBING INFORMATION

Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL CII

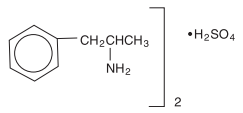
WARNING

AMPHETAMINES HAVE A HIGH POTENTIAL FOR ABUSE. ADMINISTRATION OF AMPHETAMINES FOR PROLONGED PERIODS OF TIME MAY LEAD TO DRUG DEPENDENCE AND MUST BE AVOIDED. PARTICULAR ATTENTION SHOULD BE PAID TO THE POSSIBIL TY OF SUBJECTS OBTAINING AMPHETAMINES FOR NON-THERAPEUTIC USE OR DISTRIBUTION TO OTHERS, AND THE DRUGS SHOULD BE PRESCRIBED OR DISPENSED SPARINGLY.
MISUSE OF AMPHETAMINE MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

DESCRIPTION

Detroamphetamine sulfate is he dextro isomer of the compound *d,l*-amphetamine sulfate, a sympathomimetic amine of he amphetamine group. Chemically, dextroamphetamine is *d*-alpha-methylphenethylamine, and is present in all forms of dextroamphetamine sulfate as he neutral sulfate.

Structural Formula:



Dextroamphetamine Sulfate Oral Solution is a colorless, bubblegum flavored oral solution. Each teaspoonful (5 mL) of Dextroamphetamine Sulfate Oral Solution contains 5 mg of dextroamphetamine sulfate. Inactive ingredients consist of benzoic acid, citric acid anhydrous, purified water, sodium citrate hydrous, sodium saccharin, sorbitol solution, and artificial bubble gum flavor.

CLINICAL PHARMACOLOGY

Amphetamines are noncatecholamine, sympa homimetic amines wi h CNS stimulant activity. Peripheral actions include elevations of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action.

There is ne ther specific evidence hat clearly establishes the mechanism whereby amphetamines produce mental and behavioral effects in children, nor conclusive evidence regarding how these effects relate to he condition of he central nervous system.

Pharmacokinetics

Ingestion of 10 mg of dextroamphetamine sulfate in oral solution form by heal hy volunteers produced an average peak dextroamphetamine blood level of 33.2 ng/mL. The half-life was 11.75 hours. The average urinary recovery was 38% in 48 hours.

In 12 heal hy subjects, he rate and extent of dextroamphetamine absorption were similar following administration of he sustained release capsule formulation in he fed (58 to 75 gm fat) and fasted state.

INDICATIONS AND USAGE

Dextroamphetamine Sulfate Oral Solution is indicated in:

Narcolepsy

Attention Deficit Disorder with Hyperactivity: As an integral part of a total treatment program hat typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in pediatric patients (ages 3 years to 16 years) w th a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: Moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of this syndrome should not be made w th finality when hese symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, lea ning disability, and abnormal EEG may or may not be present, and a diagnosis of central nervous system dysfunction may or may not be warranted.

CONTRAINDICATIONS

Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympa homimetic amines, glaucoma.

Agitated states.

Patients wi h a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crisis may result).

WARNINGS

Serious Cardiovascular Events

Sudden Death in Patients with Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems: ***Children and Adolescents:*** Sudden death has been reported in association wi h CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or o her serious heart problems. Al hough some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents wi h known serious structural cardiac abnormalities, cardiomyopathy, serious heart hy hm abnormalities, or o her serious cardiac problems hat may place them at increased vulnerability to the sympa homimetic effects of a stimulant drug.

Adults: Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although he role of stimulants in hese adult cases is also unknown, adults have a greater like ihood han child en of having serious structural cardiac abnormalities, cardiomyopa hy, serious heart hy hm abnormalities, coronary artery disease, or o her serious cardiac problems. Adults wi h such abnormalities should also generally not be treated with stimulant drugs (see CONTRAINDICATIONS).

Hypertension and Other Cardiovascular Conditions: Stimulant medications cause a modest increase in average blood pressure (about 2-4 mmHg) and average heart rate (about 3-6 bpm), and individuals may have larger increases. While he mean changes alone would not be expected to have short term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., hose with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular ar hy hmia (see CONTRAINDICATIONS).

Assessing Cardiovascular Status in Patients Being Treated With Stimulant Medications: Children, adolescents, or adults who are being conside ed for t eatment wi h stimulant medications should have a careful history (including assessment for a family history of sudden dea h or ventricular ar hythmia) and physical exam to assess for he presence of cardiac disease, and should receive fur her cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or o her symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

Psychiatric Adverse Events

Pre-Existing Psychosis: Administration of stimulants may exacerbate symptoms of behavior disturbance and hought disorder in patients wi h pre-existing psychotic disorder.

Bipolar Illness: Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of conce n for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment wi h stimulant, patients wi h como bid depressive symptoms should be adequately screened to determine if hey are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Emergence of New Psychotic or Manic Symptoms: Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional hinking, or mania in children and adolescents wi hout a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of t eatment may be appropriate. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients wi h events out of 3,482 exposed to me hylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression: Aggressive behavior or hostility is often observed in children and adolescents wi h ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for he treatment of ADHD. Al hough here is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be monitored for he appearance of, or worsening of, aggressive behavior or hostility.

Long-Term Suppression of Growth: Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to ei her methylphenidate or non-medication treatment groups over 14 mon hs, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 mon hs (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week hroughout he year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), wi hout evidence of grow h rebound during his period of development. Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of grow h, however, it is anticipated that they likely have his effect as well. Therefore, grow h should be monitored during treatment with stimulants, and patients who are not growing or gaining height or weight as expected may need to have heir treatment interrupted.

Seizures: There is some clinical evidence hat stimulants may lower the convulsive h eshold in patients with prior history of seizures, in patients wi h prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In he presence of seizures, he drug should be discontinued.

Visual Disturbance: Difficulties w th accommodation and blurring of vision have been reported with stimulant treatment.

PRECAUTIONS:

General: 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 he ability of he patient to engage in potentially hazardous activities such as operating machinery or vehicles; he patient should the efore be cautioned accordingly.

Prescribers or o her hea th professionals should inform patients, heir families, and heir caregivers about the benefits and risks associated wi h t eatment wi h dextroamphetamine and should counsel hem in its appropriate use. A patient Medication Guide is available for dextroamphetamine sulfate. The prescriber or health professional should instruct patients, heir families, and their caregivers to read he Medication Guide and should assist hem in understanding its contents. Patients should be given he opportunity to discuss he contents of he Medication Guide and to obtain answers to any questions hey may have. The complete text of the Medication Guide is reprinted at he end of his document.

Drug Interactions:

Acidifying agents - Gastrointestinal acidifying agents (guanethidine, reserpine, glutamic acid HCl, ascorbic acid, fruit juices, etc.) lower absorption of amphetamines. Urinary acidifying agents (ammonium chloride, sodium acid phosphate, etc.) increase he concentration of he ionized species of he amphetamine molecule, hereby increasing urinary excretion. Bo h groups of agents lower blood levels and efficacy of amphetamines.

Adrenergic blockers - Ad energic blockers are inhibited by amphetamines.

Alkalinizing agents - Gastrointestinal alkalinizing agents (sodium bicarbonate, etc.) increase absorption of amphetamines. Urinary alkalinizing agents (acetazolamide, some thiazides) increase he concentration of the non-ionized species of he amphetamine molecule, thereby decreasing urinary excretion. Both groups of agents increase blood levels and herefore potentiate the actions of amphetamines.

Antidepressants, tricyclic - Amphetamines may enhance he activity of tricyclic or sympa homimetic agents; d-amphetamine wi h desipramine or protriptyline and possibly o her tricyclics cause striking and sustained increases in he concentration of d-amphetamine in he brain; cardiovascular effects can be potentiated.

MAO inhibitors - MAOI antidep essants, as well as a metabolite of furazolidone, slow amphetamine metabolism. This slowing potentiates amphetamines, increasing heir effect on he elease of no epinephrine and o her monoamines from adrenergic nerve endings; this can cause headaches and other signs of hypertensive crisis. A variety of neurological toxic effects and malignant hyperpy exia can occur, sometimes wi h fatal results.

Antihistamines - Amphetamines may counteract the sedative effect of antihistamines.

Antihypertensives - Amphetamines may antagonize he hypotensive effects of antihypertensives.

Chlorpromazine - Chlo promazine blocks dopamine and norepinephrine reuptake, hus inhibiting he central stimulant effects of amphetamines, and can be used to treat amphetamine poisoning.

Ethosuximide - Amphetamines may delay intestinal absorption of ethosuximide.

Haloperidol - Haloperidol blocks dopamine and norepinephrine reuptake, hus inhibiting he central stimulant effects of amphetamines.

Lithium carbonate - The stimulatory effects of amphetamines may be inhibited by li hium carbonate.

Meperidine - Amphetamines potentiate the analgesic effect of meperidine.

Methenamine Therapy - Urinary excretion of amphetamines is increased, and efficacy is educed, by acidifying agents used in methenamine herapy.

Norepinephrine - Amphetamines enhance the adrenergic effect of norepinephrine.

Phenobarbital - Amphetamines may delay intestinal absorption of phenobarbital; co-administration of phenobarbital may produce a synergistic anticonvulsant action.

Phenytoin - Amphetamines may delay intestinal absorption of phenytoin; co-administration of phenytoin may produce a synergistic anticonvulsant action.

Propoxyphene - In cases of propoxyphene overdosage, amphetamine CNS stimulation is potentiated and fatal convulsions can occur.

Veratrum Alkaloids - Amphetamines inhibit the hypotensive effect of veratrum alkaloids.

Drug/Laboratory Test Interactions

Amphetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in he evening.

Amphetamines may interfe e with urinary steroid determinations.

Carcinogenesis/Mutagenesis: Mutagenicity studies and long-term studies in animals determine he carcinogenic potential of *Dextroamphetamine Sulfate* has not been performed.

Pregnancy: ***Teratogenic Effects***: Pregnancy Category C. *Dextroamphetamine Sulfate* has been shown to have embryotoxic and teratogenic effects when administered to A/Jax mice and C57BL mice in doses approximately 41 times he maximum human dose. Embryotoxic effects were not seen in New Zealand white rabbits given the drug in doses 7 times he human dose nor in rats given 12.5 times the maximum human dose. While here a e no adequate and well-controlled studies in pregnant women, here has been one report of severe congenital bony deformity, tracheoesophageal fistula, and anal atresia (VATER association) in a baby bo n to a woman who took dextroamphetamine sulfate with lovastatin during he first trimester of pregnancy. *Dextroamphetamine Sulfate* should be used during pregnancy only if the potential benefit justifies he potential risk to the fetus.

Nonteratogenetic Effects: Infants bo n to mo hers dependent on amphetamines have an increased risk of premature delivery and low bir h weight. Also, hese infants may experience symptoms of withdrawal as demonstrated by dysphoria, including agitation, and significant lassitude.

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

Pediatric Use: Long-term effects of amphetamines in pediatric patients have not been well established.

Amphetamines are not ecommended for use in pediatric patients under 3 years of age wi h Attention Deficit Disorder with Hyperactivity described under INDICATIONS AND USAGE.

Clinical experience suggests hat in psychotic children, administration of amphetamines may exacerbate symptoms of behavior disturbance and hought disorder.

Amphetamines have been reported to exacerbate motor and phonic tics and Tourette's syndrome. Therefore, clinical evaluation for tics and Tourette's syndrome in children and heir families should precede use of stimulant medications.

Data a e inadequate to determine whe her chronic administration of amphetamines may be associated wi h growth inhibition; therefore, growth should be monitored during treatment.

Drug treatment is not indicated in all cases of Attention Deficit Disorder wi h Hyperactivity and should be considered only in light of the complete history and evaluation of the child. The decision to prescribe amphetamines should depend on he physician's assessment of he chronicity and severity of he child's symptoms and heir appropriateness for his or her age. Prescription should not depend solely on he p esence of one or more of he behavioral characteristics.

When hese symptoms are associated wi h acute stress reactions, treatment wi h amphetamines is usually not indicated.

ADVERSE REACTIONS

Cardiovascular: Palpitations, tachycardia, elevation of blood pressure. There have been isolated reports of cardiomyopa hy associated wi h chronic amphetamine use.

Central Nervous System: Psychotic episodes at recommended doses (rare), overstimulation, estlessness, dizziness, insomnia, euphoria, dyskinesia, dysphoria, tremor, headache, exacerbation of motor and phonic tics and Tourette's syndrome.

Gastrointestinal: Dryness of he mou h, unpleasant taste, diar hea, constipation, o her gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects.

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

DRUG ABUSE AND DEPENDENCE

Dextroamphetamine sulfate is a Schedule II controlled substance.

Amphetamines have been extensively abused. Tolerance, extreme psychological dependence and severe social disability have occurred. There are reports of patients who have increased the dosage to many times hat recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on he sleep EEG.

Manifestations of chronic intoxication wi h amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia. This is rare with oral amphetamines.

OVERDOSAGE

Individual patient response to amphetamines varies widely. While toxic symptoms occasionally occur as an idiosyncrasy at doses as low as 2 mg, they a e rare wi h doses of less han 15 mg; 30 mg can produce severe reactions, yet doses of 400 to 500 mg are not necessarily fatal.

In rats, he oral LD_{50} of dextroamphetamine sulfate is 96.8 mg/kg.

Manifestations of acute overdosage with amphetamines include restlessness, tremor, hypereflexia, habdomyolysis, rapid respiration, hype pyrexia, confusion, assaultiveness, hallucinations, panic states.

Fatigue and dep ession usually follow the central stimulation.

Cardiovascular effects include ar hythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diar hea and abdominal cramps. Fatal poisoning is usually proceeded by convulsions and coma.

TREATMENT

Consult wi h a Certified Poison Control Center for up-to-date guidance and advice. Management of acute amphetamine intoxication is la gely symptomatic and includes gastric lavage, administration of activated charcoal, administration of a ca hartic, and sedation. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in his regard. Acidification of the urine increases amphetamine excretion, but is believed to increase risk of acute renal failure if myoglobinuria is present. If acute, severe hypertension complicates amphetamine overdosage, administration of intravenous phentolamine (Bedford Laboratories) has been suggested. However, a gradual drop in blood pressure will usually esult when sufficient sedation has been achieved.

Chlorpromazine antagonizes he central stimulant effects of amphetamines and can be used to treat amphetamine intoxication.

DOSAGE AND ADMINISTRATION

Amphetamines should be administered at he lowest effective dosage and dosage should be individually adjusted. Late evening doses should be avoided because of he esulting insomnia.

Narcolepsy: Usual dose is 5 mg to 60 mg per day in divided doses, depending on the individual patient response.

Na colepsy seldom occurs in children under 12 years of age; however, when it does, Dextroamphetamine Sulfate Oral Solution may be used. The suggested initial dose for patients aged 6 to 12 is 5 mg daily; daily dose may be raised in increments of 5 mg at weekly intervals until optimal response is obtained. In patients 12 years of age and older, start with 10 mg daily; daily dosage may be raised in increments of 10 mg at weekly intervals until optimal response is obtained. If bo hersome adverse reactions appear (e.g., insomnia or anorexia), dosage should be reduced. Give first dose on awakening; additional doses (1 or 2) at intervals of 4 to 6 hours.

Attention Deficit Disorder with Hyperactivity: Not recommended for pediatric patients under 3 years of age.

In pediatric patients from 3 to 5 years of age, start wi h 2.5 mg daily; daily dosage may be raised in increments of 2.5 mg at weekly intervals until optimal esponse is obtained.

In pediatric patients 6 years of age and older, start wi h 5 mg once or twice daily; daily dosage may be raised in increments of 5 mg at weekly intervals until optimal response is obtained. Only in rare cases will it be necessary to exceed a total of 40 mg per day.

Give first dose on awakening; additional doses (1 or 2) at intervals of 4 to 6 hours.

Where possible, drug administration should be interrupted occasionally to determine if the e is a recurrence of behavioral symptoms sufficient to require continued herapy.

HOW SUPPLIED

Dextroamphetamine Sulfate Oral Solution, 5mg/5mL is a colorless, bubblegum flavored oral solution, available in containers of 16 fluid ounces, NDC 46672-646-16.

Store at 20° - 25°C (68° - 77°F) (See USP Controlled Room Temperature). Dispense in a tight, light resistant container.

Manufactured by:
Mikart, Inc.
Atlanta, Georgia, 30318

Manufactured for:
Outlook Pharmaceuticals Inc.
Cincinnati, OH 45209

Code 983Z00 Rev. 10/07

46672646

Dextroamphetamine Sulfate Oral Solution
5 mg/5 mL CII

Code 983Z00 Rev. 10/07

MEDICATION GUIDE

Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL CII

Read the Medication Guide that comes with Dextroamphetamine Sulfate Oral Solution before you or your child starts taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your or your child's treatment with Dextroamphetamine Sulfate Oral Solution.

What is the most important information I should know about Dextroamphetamine Sulfate Oral Solution?

The following have been reported with use of Dextroamphetamine Sulfate Oral Solution and other stimulant medicines.

1. Heart-related problems:

- **sudden death in patients who have heart problems or heart defects**
- **stroke and heart attack in adults**
- **increased blood pressure and heart rate**

Tell your doctor if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

Your doctor should check you or your child carefully for heart problems before starting Dextroamphetamine Sulfate Oral Solution.

Your doctor should check your or your child's blood pressure and heart rate regularly during treatment with Dextroamphetamine Sulfate Oral Solution.

Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking Dextroamphetamine Sulfate Oral Solution.

2. Mental (Psychiatric) problems:

All Patients

- **new or worse behavior and thought problems**
- **new or worse bipolar illness**
- **new or worse aggressive behavior or hostility**

Children and Teenagers

- **new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms**

Tell your doctor about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.

Call your doctor right away if you or your child have any new or worsening mental symptoms or problems while taking Dextroamphetamine Sulfate Oral Solution, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What Is Dextroamphetamine Sulfate Oral Solution?

Dextroamphetamine Sulfate Oral Solution is a central nervous system stimulant prescription medicine. **It is used for the treatment of Attention-Deficit Hyperactivity Disorder(ADHD)**. Dextroamphetamine Sulfate Oral Solution may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

Dextroamphetamine Sulfate Oral Solution should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

Dextroamphetamine Sulfate Oral Solution is also used in the treatment of a sleep disorder called narcolepsy.

Dextroamphetamine Sulfate Oral Solution is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep Dextroamphetamine Sulfate Oral Solution in a safe place to prevent misuse and abuse. Selling or giving away Dextroamphetamine Sulfate Oral Solution may harm others, and is against the law.

Tell your doctor if you or your child have (or have a family history of) ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take Dextroamphetamine Sulfate Oral Solution?

Dextroamphetamine Sulfate Oral Solution should not be taken if you or your child:

- have heart disease or hardening of the arteries
- have moderate to severe high blood pressure
- have hyperthyroidism
- have an eye problem called glaucoma
- are very anxious, tense, or agitated
- have a history of drug abuse
- are taking or have taken within the past 14 days an antidepression medicine called a monoamine oxidase inhibitor or MAOI.
- is sensitive to, allergic to, or had a reaction to other stimulant medicines

Dextroamphetamine Sulfate Oral Solution is not recommended for use in children less than 3 years old.

Dextroamphetamine Sulfate Oral Solution may not be right for you or your child. Before starting Dextroamphetamine Sulfate Oral Solution tell your or your child's doctor about all health conditions (or a family history of) including:

- heart problems, heart defects, high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- tics or Tourette's syndrome
- thyroid problems
- seizures or have had an abnormal brain wave test (EEG)

Tell your doctor if you or your child is pregnant, planning to become pregnant, or breastfeeding.

Can Dextroamphetamine Sulfate Oral Solution be taken with other medicines?

Tell your doctor about all of the medicines that you or your child take including prescription and nonprescription medicines, vitamins, and herbal supplements. Dextroamphetamine Sulfate Oral Solution and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking Dextroamphetamine Sulfate Oral Solution.

Your doctor will decide whether Dextroamphetamine Sulfate Oral Solution can be taken with other medicines.

Especially tell your doctor if you or your child takes:

- anti-depression medicines including MAOIs
- blood pressure medicines
- antacids
- seizure medicines

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your doctor and pharmacist.

Do not start any new medicine while taking Dextroamphetamine Sulfate Oral Solution without talking to your doctor first.

How should Dextroamphetamine Sulfate Oral Solution be taken?

- **Take Dextroamphetamine Sulfate Oral Solution exactly as prescribed**. Your doctor may adjust the dose until it is right for you or your child.
- Dextroamphetamine Sulfate Oral Solution is usually taken two to three times a day. The first dose is usually taken in the morning. One or two more doses may be taken during the day, 4 to 6 hours apart.
- From time to time, your doctor may stop Dextroamphetamine Sulfate Oral Solution treatment for a while to check ADHD symptoms.
- Your doctor may do regular checks of the blood, heart, and blood pressure while taking Dextroamphetamine Sulfate Oral Solution. Children should have their height and weight checked often while taking Dextroamphetamine Sulfate Oral Solution. Dextroamphetamine Sulfate Oral Solution treatment may be stopped if a problem is found during these check-ups.
- **If you or your child takes too much Dextroamphetamine Sulfate Oral Solution or overdoses, call your doctor or poison control center right away, or get emergency treatment.**

What are possible side effects of Dextroamphetamine Sulfate Oral Solution?

See "**What is the most important information I should know about Dextroamphetamine Sulfate Oral Solution?**" for information on reported heart and mental problems.

Other serious side effects include:

- slowing of growth (height and weight) in children
- seizures, mainly in patients with a history of seizures
- eyesight changes or blurred vision

Common side effects include:

- fast heart beat
- tremors
- trouble sleeping
- stomach upset
- dry mouth
- decreased appetite
- headache
- dizziness
- weight loss

Dextroamphetamine Sulfate Oral Solution may affect you or your child's ability to drive or do other dangerous activities.

Talk to your doctor if you or your child has side effects that are bothersome or do not go away.

This is not a complete list of possible side effects. Ask your doctor or pharmacist for more information

How should I store Dextroamphetamine Sulfate Oral Solution?

- Store Dextroamphetamine Sulfate Oral Solution in a safe place at room temperature, 68 to 77° F (20 to 25° C). Protect from light.
- Keep Dextroamphetamine Sulfate Oral Solution and all medicines out of the reach of children.

General information about Dextroamphetamine Sulfate Oral Solution

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Dextroamphetamine Sulfate Oral Solution for a condition for which it was not prescribed. Do not give Dextroamphetamine Sulfate Oral Solution to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about Dextroamphetamine Sulfate Oral Solution. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Dextroamphetamine Sulfate Oral Solution that was written for healthcare professionals. For more information about Dextroamphetamine Sulfate Oral Solution, please contact Outlook Pharmaceuticals at 1-800-287-8365.

What are the ingredients in Dextroamphetamine Sulfate Oral Solution?

Active Ingredient: dextroamphetamine sulfate

Inactive Ingredients: benzoic acid, citric acid anhydrous, purified water, sodium citrate hydrous, sodium saccharin, sorbitol solution, and artificial bubble gum flavor.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by: Mikart, Inc.,
Atlanta, GA 30318

Revised October 2007

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-776 Date of Submission: April 28, 2006

Applicant's Name: Outlook Pharmaceuticals, Inc.

Established Name: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

Labeling Deficiencies:

1. CONTAINER (473 mL)

   a. Delete "(b) (4)

   b. Increase the expression of strength.

   c. Revise the storage temperature statement to read "Store at 20^0 to 25^0C (68^0 to 77^0F)[see USP controlled room temperature]".

   d. Please confirm whether the (b) (4) printed liner with red highlighted letter satisfies 21 CFR 1302.06 (Sealing of controlled substances).

   e. Relocate the bottom statement on the principal display panel to the side panel and revise to read "Each 5 mL contains dextroamphetamine sulfate, 5 mg."

   f. Include the statement "PHARMACIST: Dispense Medication Guide with the Drug Product".

2. INSERT

   a. New labeling was approved for Dexedrine Spansule Sustained-Release Capsules on May 1, 2007. Prior to the withdrawal of Dexedrine Elixir from the market, it shared the insert labeling with Dexedrine Spansule and Dexedrine Tablets. The new safety information approved for Dexedrine appears to apply for all formulations including the oral solution. Please review the approved labeling for Dexedrine Spansule available on the Drugs@FDA website and revise accordingly.

   b. CLINICAL PHARMACOLOGY

      Revise the first paragraph to read as follows:

      "Ingestion of 10 mg of dextroamphetamine sulfate in oral solution form by healthy volunteers produced an average peak dextroamphetamine blood level of 33.2 ng/mL. The half-life was 11.75 hours. The average urinary recovery was 38% in 48 hours."

3. MEDICATION GUIDE

   a. Dexedrine Spansule and Tablet are approved with a Medication Guide. The medication guide should also be made available for proposed dextroamphetamine oral solution.

   b. Please indicate the number medication guides you intend to include for each bottle and how they will be made available.

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. MODEL LABELING: Dexedrine Spansule Sustained-Release Capsules, NDA 17-078/S-042,

Approved May 1, 2007. Dexedrine Elixir is listed as the reference listed drug however, it is no longer being marketed by the company. It was discontinued in 1988 but not for safety reasons.

2. INACTIVE INGREDIENTS: Consistent with the application.

3. PATENTS/EXCLUSIVITIES: None

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
USP: The solution is not USP but dextroamphetamine sulfate is. Storage recommendation is to preserve in well closed container.
- **RLD: Store between 15^0 and 30^0 C (59^0 and 86^0F) Dispense in a tight, light-resistant container.**
- **ANDA: Store between 20^0 and 25^0 C (68^0 and 77^0F)[see USP].**

5. DISPENSING STATEMENT COMPARISON
- **RLD: Dispense in a tight, light resistant container.**
- **ANDA: Dispense in a tight, light resistant container.**

6. PACKAGE CONFIGURATION
- **RLD: None**
- **ANDA: 473 mL bottle**

7. CONTAINER/CLOSURE
HDPE bottles closed with (b) (4) caps with (b) (4) printed liner with red highlighted letter. The bottle is designed to protect the product from light and excess moisture.

8. FINISHED DOSAGE FORM
- **ANDA: Colorless, bubblegum flavored oral solution.**

9. MANUFACTURER

Mikart Inc., 2090 Marietta Blvd. Atlanta, GA 30318

10. Pharmokinetics

From: Davit, Barbara M
Sent: Friday, June 29, 2007 1:47 PM
To: Lee, Koung U
Subject: RE: Alcohol

Koung:

Ethanol is not known to interact with amphetamines. I don't think that a PK study is necessary.

Barbara

From: Lee, Koung U
Sent: Friday, June 29, 2007 12:28 PM
To: Davit, Barbara M
Subject: Alcohol

Hi Barbara,

Can alcohol affect the pharmacokinetics of a drug product? I have an alcohol free dextroamphetamine solution application (40-776). The reference listed drug, Dexedrine Elixir, contains 10% alcohol. Should I ask the firm to provide PK data to support the PK information in the RLD labeling?

Your help is much appreciated. Thanks Barbara.

Koung

11. Mikart POC: Pieter Groenewoud, 404-351-4510 x 301, fax 404-352-0451

Date of Review: June 21, 2007	**Date of Submission: April 28, 2006**
Primary Reviewer: Koung Lee	**Date:**
Team Leader: Lillie Golson	**Date:**

NA1

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Koung Lee
7/2/2007 02:18:58 PM
LABELING REVIEWER

Lillie Golson
7/3/2007 12:24:23 PM
LABELING REVIEWER

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-776 Date of Submission: September 14, 2007

Applicant's Name: Outlook Pharmaceuticals, Inc.

Established Name: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

Labeling Deficiencies:

1. CONTAINER (473 mL)

   a. Further increase the prominence of the expression of strength.

   b. Revise the storage temperature statement to read "Store at 20° - 25°C (68° - 77°F) (See USP Controlled Room Temperature)".

2. INSERT

   a. BOXED WARNING

      Correct the spelling of "THERAPEUTIC" in the last sentence of the first paragraph.

   b. DESCRIPTION

      i. The inactive ingredients do not need to be capitalized.

      ii. Add "hydrous" at end of "sodium citrate".

   c. CLINICAL PHARMACOLOGY

      Relocate the first paragraph to replace the first paragraph in the "Pharmacokinetics" subsection.

   d. INDICATIONS AND USAGE

      Replace "emotionally" with "emotional" in the first sentence of the "Attention Deficit Disorder with Hyperactivity" subsection.

   e. WARNINGS

      i. Add "s" at the end of "*Adolescent*" in the subsection heading "Sudden Death in…Heart Problems: *Children and Adolescents*".

      ii. In the first sentence under "Assessing Cardiovascular Status in…with Stimulant Medications:" add an "s" at the end of "medication" in the first sentence.

      iii. In the penultimate sentence in the "Long-Term Suppression of Growth" subsection, replace "or" with "no".

   f. PRECAUTIONS

      i. Add the following to appear as the second paragraph in the "Information for Patients" subsection:

         Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with dextroamphetamine and should counsel them in its appropriate use. A patient Medication Guide is available for dextroamphetamine sulfate. The prescriber or health professional should instruct patients, their families, and their caregivers to

read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

ii. In the second sentence of the "*Alkalinizing agents*" subsection, replace "alkalizing" with "alkalinizing".

iii. Carcinogenesis/Mutagenesis

Delete "(b) (4)".

iv. Pregnancy-Teratogenic Effects

Delete "(b) (4)" in the first and last sentence.

v. Pediatric Use

In the second sentence of the third paragraph, delete the "s" at the end of "evaluations".

g. DOSAGE AND ADMINISTRATION (Narcolepsy)

i. Revise the first sentence to read "Usual dose is 5 mg to 60 mg per day…"

ii. In the second sentence of the second paragraph, revise to read "…aged 6 to 12 is 5 mg daily…"

iii. Add the following at the end of the second paragraph:

"Give first dose on awakening; additional doses (1 or 2) at intervals of 4 to 6 hours."

h. HOW SUPPLIED

Revise the storage temperature statement to read "Store at 20^{o} - 25^{o}C (68^{o} - 77^{o}F) (See USP Controlled Room Temperature)".

3. MEDICATION GUIDE

a. Heart-related problems:

Revise the third paragraph to read "Your doctor should check your or your child's blood pressure…"

b. What is Dextroamphetamine Sulfate Oral Solution

Delete the second sentence in the first pagraph.

c. Who should not take Dextroamphetamine Sulfate Oral Soution?

Delete the fourth bulleted statement (b) (4)".

d. How should Dextroamphetamine Sulfate Oral Solution be taken?

Revise the second paragrah to read as follows:

Dextroamphetamine Sulfate Oral Solution is usually taken two to three times a day. The first dose is usually taken in the morning. One or two more doses may be taken during the day, 4 to 6 hours apart.

Please revise your labeling as described above and submit electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. **MODEL LABELING: Dexedrine Spansule Sustained-Release Capsules, NDA 17-078/S-042, Approved May 1, 2007. Dexedrine Elixir is listed as the reference listed drug however, it is no longer being marketed by the company. It was discontinued in 1988 but not for safety reasons.**

2. **INACTIVE INGREDIENTS: Consistent with the application except firm is asked to specify sodium citrate to read as sodium citrate hydrous.**

3. **PATENTS/EXCLUSIVITIES: None**

4. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON**
   USP: The solution is not USP but dextroamphetamine sulfate is. Storage recommendation is to preserve in well closed container.
   - **RLD: Store between 15^0 and 30^0 C (59^0 and 86^0F) Dispense in a tight, light-resistant container.**
   - **ANDA: Store between 20^0 and 25^0 C (68^0 and 77^0F)[see USP].**

5. **DISPENSING STATEMENT COMPARISON**
   - **RLD: Dispense in a tight, light resistant container.**
   - **ANDA: Dispense in a tight, light resistant container.**

6. **PACKAGE CONFIGURATION**
   - **RLD: None**
   - **ANDA: 473 mL bottle**

7. **CONTAINER/CLOSURE**
   HDPE bottles closed with (b) (4) caps with tamper evident (b) (4) printed liner with red highlighted letter. The bottle is designed to protect the product from light and excess moisture.

8. **FINISHED DOSAGE FORM**
   - **ANDA: Colorless, bubblegum flavored oral solution.**

9. **MANUFACTURER**

Mikart Inc., 2090 Marietta Blvd. Atlanta, GA 30318

10. Pharmacokinetics

From: Davit, Barbara M
Sent: Friday, June 29, 2007 1:47 PM
To: Lee, Koung U
Subject: RE: Alcohol

Koung:

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From: Lee, Koung U
Sent: Friday, June 29, 2007 12:28 PM
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Hi Barbara,

Can alcohol affect the pharmacokinetics of a drug product? I have an alcohol free dextroamphetamine solution application (40-776). The reference listed drug, Dexedrine Elixir, contains 10% alcohol. Should I ask the firm to provide PK data to support the PK information in the RLD labeling?

Your help is much appreciated. Thanks Barbara.

Koung

---

11. Mikart POC: Pieter Groenewoud, 404-351-4510 x 301, fax 404-352-0451

Date of Review: October 4, 2007 **Date of Submission: Septebmer 14, 2007**

Primary Reviewer: Koung Lee **Date:**

Team Leader: Lillie Golson **Date:**

NA2

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Koung Lee
10/15/2007 03:10:39 PM
LABELING REVIEWER

Lillie Golson
10/15/2007 04:16:43 PM
LABELING REVIEWER

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-776 Date of Submission: November 14, 2007

Applicant's Name: Outlook Pharmaceuticals, Inc.

Established Name: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

All labeling pieces submitted electronically in final print format. SPL also submitted for the insert.

	Submission Date	Recommendation
Container (473 mL)	**11/14/2007**	**Acceptable for Approval**
Insert	**11/14/2007**	**Acceptable for Approval**
Medication Guide	**11/14/2007**	**Acceptable for Approval**

FOR THE RECORD:

1. **MODEL LABELING: Dexedrine Spansule Sustained-Release Capsules, NDA 17-078/S-042, Approved May 1, 2007. Dexedrine Elixir is listed as the reference listed drug however, it is no longer being marketed by the company. It was discontinued in 1988 but not for safety reasons.**

2. **INACTIVE INGREDIENTS: Consistent with the application.**

3. **PATENTS/EXCLUSIVITIES: None**

4. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON**
   USP: The solution is not USP but dextroamphetamine sulfate is. Storage recommendation is to preserve in well closed container.
   - **RLD: Store between 15^0 and 30^0 C (59^0 and 86^0F) Dispense in a tight, light-resistant container.**
   - **ANDA: Store between 20^0 and 25^0 C (68^0 and 77^0F)[see USP].**

5. **DISPENSING STATEMENT COMPARISON**
   - **RLD: Dispense in a tight, light resistant container.**
   - **ANDA: Dispense in a tight, light resistant container.**

6. **PACKAGE CONFIGURATION**
   - **RLD: None**
   - **ANDA: 473 mL bottle**

7. **CONTAINER/CLOSURE**
   HDPE bottles closed with (b) (4) caps with (b) (4) printed liner (tamper indicating) with red highlighted letter. The bottle is designed to protect the product from light and excess moisture.

8. **FINISHED DOSAGE FORM**
   - **ANDA: Colorless, bubblegum flavored oral solution.**

9. **MANUFACTURER**

   Mikart Inc., 2090 Marietta Blvd. Atlanta, GA 30318

10. **Pharmokinetics**

From: Davit, Barbara M

Sent: Friday, June 29, 2007 1:47 PM
To: Lee, Koung U
Subject: RE: Alcohol

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Your help is much appreciated. Thanks Barbara.

Koung

---

11. Mikart POC: Pieter Groenewoud, 404-351-4510 x 301, fax 404-352-0451

Date of Review: January 2, 2008 **Date of Submission: November 14, 2007**

Primary Reviewer: Koung Lee **Date:**

Team Leader: Lillie Golson **Date:**

AP

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Koung Lee
1/7/2008 01:40:01 PM
LABELING REVIEWER

Lillie Golson
1/7/2008 03:53:45 PM
LABELING REVIEWER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

CHEMISTRY REVIEWS

ANDA #40-776

Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

Outlook Pharmaceuticals, Inc.

Sema Basaran, Ph.D.
Office of Generic Drugs, Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA # 40-776

2. REVIEW #: 1

3. REVIEW DATE: 8/17/06

4. REVIEWER: Sema Basaran, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	April 28, 2006
Acknowledgement Letter	May 1, 2006

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	April 28, 2006

7. NAME & ADDRESS OF APPLICANT:

Name:	Outlook Pharmaceuticals Inc.
Address:	P.O.Box 9319 Cincinnati, OH 45209
Representative:	Mikart, Inc. Attention : Pieter Groenewoud, Vice President,R&D Chattahoochee Avenue Atlanta, GA 30318

CHEMISTRY REVIEW

Chemistry Review Data Sheet

Telephone: (404) 351-4510 x 301
Fax: (404) 352-0451

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA
b) Non-Proprietary Name (USAN): Dextroamphetamine Sulfate Oral Solution, 5mg/5mL
c) Code Name/# (ONDC only): NA
d) Chem. Type/Submission Priority (ONDC only): NA

- Chem. Type:
- Submission Priority:

9. LEGAL BASIS FOR SUBMISSION: The RLD is Dexedrine® Elixir, 5 mg/5 mL the subject of NDA # 83-902 held by Glaxo Smith Kline m. The firm filed a Paragraph I statement. There are no patents or exclusivity.

10. PHARMACOL. CATEGORY: Anti-narcoleptic and Anti ADD with Hyperactivity

11. DOSAGE FORM: Oral Solution

12. STRENGTH/POTENCY: 5 mg/5 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

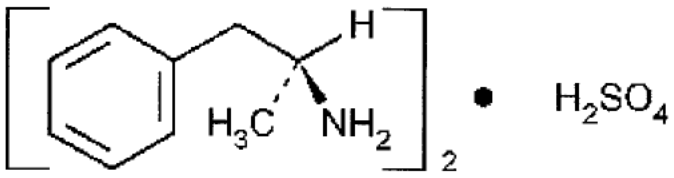
_____X Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Dextroamphetamine Sulfate , USP

Dextroamphetamine Sulfate , USP
$(C_9H_{13}N)_2 \cdot H_2SO_4$; MW 368.49

Benzeneethanamine, a-methyl-, (S)-, sulfate (2:1).
(+)-a-Methylphenethylamine sulfate (2:1)
CAS registry number: [51-63-8].



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	adequate	9-6-06	Reviewed by S.Basaran
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

18. STATUS:

OGD:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Pending		
Methods Validation	NA – program discontinued		
Labeling	Pending		
Bioequivalence	Pending		
EA	NA		
Radiopharmaceutical	NA		

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA # 40-776

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Recommended for Approval-Minor

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Dextroamphetamine Sulfate drug substance is a white to off white powder. 1 part dissolves in 10 parts water, in 500 parts of 95% alcohol. The pH of 5% aqueous solution is 5.0-6.0. Dextroamphetamine sulfate is the dextrorotatory isomer of amphetamine sulfate with a specific rotation of +20° to +23.5°.

Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL is supplied as clear, colorless, sugar and alcohol free liquid containing 5 mg Dextroamphetamine Sulfate per 5 mL. The manufacturing process can be described as (b) (4) (b) (4). The finished drug product is packaged in 16 ounce bottles. Accelerated stability testing support the firm's 24 month expiration dating period. The firm also provided 3 months of room temperature stability data. Finished product is stored at CRT (20 -25°C) in tight, light resistant container/closure systems.

The drug substance is a USP product, however the drug product is not covered by USP or PF monograph to date.

B. Description of How the Drug Product is Intended to be Used

N/A

C. Basis for Approvability or Not-Approval Recommendation

The application is not approvable. A minor CMC deficiency letter will be issued. Issues to be resolved include drug substance, clarification regarding proposed in-process testing, impurity specifications and manufacturing procedures. Also labeling, bioequivalence and EER are pending.

Following this page, 20 pages withheld in full - (b)(4)

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert:
Under review

B. Environmental Assessment Or Claim Of Categorical Exclusion:
Refer to Section 1.12.5. on page 6. A Categorical exclusion statement is included for the environmental impact analysis statement based on 21 CFR, 25.31(a). Satisfactory.

III. List Of Deficiencies To Be Communicated

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-776 APPLICANT: Outlook Pharmaceuticals, Inc.

DRUG PRODUCT: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL.

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. (b) (4)
2.
3.
4.
5.
6.
7.
8.
9.

11. (b) (4)

11.

12.

13.

14.

15.

16.

17.

18.

19.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate covers.

A satisfactory CGMP compliance evaluation for the firms referenced in the ANDA is required for approval. We have requested an evaluation from the Division of Manufacturing and Product Quality.

Sincerely yours,

Read for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-776
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-645/S.Basaran/8/25/06 C. Basaran 9/27/06
HFD-645/S.Furness/SRead for/9/25/06 Rad 9/27/06
HFD-617/Y.Kong/9-26-06 YK 9/27/06

F/T by: Rad 9/27/06

V:\FIRMSANZ\Outlook Pharmaceuticals\LTRS&REV\40776N01.RSB.doc

TYPE OF LETTER: NOT APPROVABLE - MINOR

ANDA #40-776

Dextroamphetamine Sulfate Oral Solution 5 mg/5 mL

Outlook Pharmaceuticals, Inc.

Sema Basaran, Ph.D.
Office of Generic Drugs, Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA # 40-776

2. REVIEW #: 2

3. REVIEW DATE: 5/1/07 ; 1/23/08

4. REVIEWER: Sema Basaran, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Firm:	
Original Submission	April 28, 2006
Telephone Amendment:	July 7, 2006
Minor Amendment:	March 23, 2007
FDA:	
Acknowledgement Letter	May 1, 2006
Minor Amendment letter	September 28, 2006

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendment	March 23, 2007
Telephone Amendment	May 22, 2007
Telephone Amendment	June 1, 2007
Telephone Amendment	January 16, 2008

7. NAME & ADDRESS OF APPLICANT:

Name: Outlook Pharmaceuticals Inc.

Chemistry Review Data Sheet

Address:	P.O.Box 9319 Cincinati, OH 45209
Representative:	Mikart, Inc. Attention to: Pieter Groenewoud Chattahoochee Avenue Atlanta, GA 30318
Telephone:	(404)-351-4510 x 301

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA
b) Non-Proprietary Name (USAN): Dextroamphetamine Sulfate Oral Solution, 5mg/5mL
c) Code Name/# (ONDC only): NA
d) Chem. Type/Submission Priority (ONDC only): NA

- Chem. Type:
- Submission Priority:

9. LEGAL BASIS FOR SUBMISSION: The RLD is Dexedrine® Elixir, 5 mg/5 mL the subject of NDA # 83-902 held by GlaxoSmithKline. The firm filed a Paragraph I statement. There are no patents or exclusivity.

10. PHARMACOL. CATEGORY: Anti-narcoleptic and Anti ADD with Hyperactivity

11. DOSAGE FORM: Oral Solution

12. STRENGTH/POTENCY: 5 mg/5 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __X_Rx ___OTC

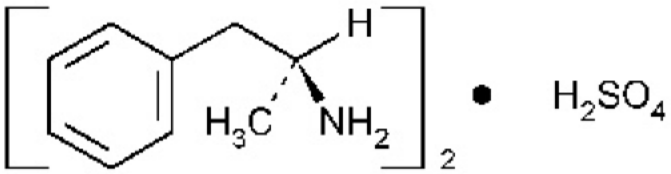
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

_____X Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Dextroamphetamine Sulfate , USP

Dextroamphetamine Sulfate , USP
$(C_9H_{13}N)_2 \cdot H_2SO_4$; MW 368.49
Benzeneethanamine, a-methyl-, (S)-, sulfate (2:1).
(+)-a-Methylphenethylamine sulfate (2:1)
CAS registry number: [51-63-8].



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	adequate	5/15/07	Reviewed by S. Basaran
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF

3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

18. STATUS:

OGD:

CONSULTS/ CMC RELATED REVIEWS	**RECOMMENDATION**	**DATE**	**REVIEWER**
Microbiology	NA		
EES	Acceptable	3/15/07	S.Ferguson
Methods Validation	NA – program discontinued		
Labeling	Acceptable	1/7/08	
Bioequivalence	Acceptable	7/6/07	
EA	NA		
Radiopharmaceutical	NA		

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes _x___ No If no, explain reason(s) below: Minor Amendment

The Chemistry Review for ANDA # 40-776

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable with respect to CMC.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Dextroamphetamine Sulfate drug substance is a white to off white powder. 1 part dissolves in 10 parts water, in 500 parts of 95% alcohol. The pH of 5% aqueous solution is 5.0-6.0. Dextroamphetamine sulfate is the dextrorotatory isomer of amphetamine sulfate with a specific rotation of +20º to +23.5º.

Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL is supplied as clear, colorless, sugar and alcohol free liquid containing 5 mg Dextroamphetamine Sulfate per 5 mL. The manufacturing process can be described as (b) (4) (b) (4). The finished drug product is packaged in 16 ounce bottles. Accelerated and stability testing support the firm's 24 month expiration dating period. The firm also provided 3 months of room temperature stability data.

The drug substance is a USP product, however the drug product is not covered by a USP or PF monograph to date.

B. Description of How the Drug Product is Intended to be Used

N/A

C. Basis for Approvability or Not-Approval Recommendation

The application is approvable with respect to CMC.

Following this page, 24 pages withheld in full - (b)(4)

: ANDA 40-776
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-645/S.Basaran/5/7/07; 1-23-08

HFD-645/S.Furness/6/5/07

HFD-617/TLiu/6/5/07 & 1/7/08

V:\FIRMSANZ\Outlook\LTRS&REV\40776N02.RSB.doc

TYPE OF LETTER: APPROVABLE

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Sema Basaran
1/28/2008 04:27:05 PM
CHEMIST

Damaris Maldonado
1/28/2008 07:00:48 PM
CHEMIST

Theresa Liu
1/29/2008 08:54:22 AM
CSO

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	40-776
Drug Product Name	Dextroamphetamine Sulfate Oral Solution
Strength(s)	5 mg/5 mL
Applicant Name	Outlook Pharmaceuticals, Inc.
Address	P.O. Box 9319, Cincinnati, OH 45209
Applicant's Point of Contact	Pieter Groenewoud
Contact's Telephone Number	404-351-4510 x301
Contact's Fax Number	513-533-3425
Original Submission Date(s)	April 28, 2006
Submission Date(s) of Amendment(s) Under Review	N/A
Reviewer	Devvrat Patel
Study Number (s)	N/A
Study Type (s)	
Strength (s)	
Clinical Site	N/A
Clinical Site Address	
Analytical Site	N/A
Analytical Site Address	

I. Executive Summary

The firm has requested a waiver of *in vivo* bioequivalence requirements for its test product, dextroamphetamine sulfate oral solution, 5 mg/5 mL. The reference listed drug (RLD) is Dexedrine® Elixir, 5 mg/5 mL, manufactured by GlaxoSmithKline. Dexedrine® Elixir is listed in the Orange Book under Discontinued Drug Products. As per the Citizen's Petition (2006P-0125/CP1), Dexedrine® Elixir was not withdrawn for sale for reasons of safety or effectiveness. All inactive ingredients used in the test formulation are within the listed levels in the Inactive Ingredient Guide.

It is a DESI drug. A waiver of in vivo bioequivalence requirements for the test product is granted.

II. Table of Contents

III. Submission Summary

A. Drug Product Information

Test Product	Dextroamphetamine Sulfate Oral Solution
Reference Product	Dexedrine® Elixir, 5 mg/5 mL (Currently listed under Discontinued Drug Products in Orange Book)
NDA No.	83-902
RLD Manufacturer	GlaxoSmithKline
RLD Approval Date	Approved prior to 1/1/1982
Indication	Indicated for treatment of narcolepsy, attention deficit disorder with hyperactivity, or for exogenous obesity.
	Dexedrine® is listed in the Orange Book under Discontinued Drug Products. A Citizen's Petition (2006P-0125/CP1) was submitted by Lachman Consultant Services on 3/17/2006 for a request to file ANDA for dextroamphetamine sulfate oral solution, 5 mg/5 mL. A memorandum issued on 2/22/2007 from OGD indicated that Dexedrine® Elixir, NDA 83-902, approved on 2/26/1976 was not withdrawn from sale for reasons of safety or effectiveness.

B. Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	
Single-dose fed	No	
Steady-state	No	
In vitro dissolution	No	
Waiver requests	Yes	1
BCS Waivers	No	
Vasoconstrictor Studies	No	
Clinical Endpoints	No	
Failed Studies	No	
Amendments	No	

C. Pre-Study Bioanalytical Method Validation:

N/A

D. In Vivo Studies:

N/A

E. Formulation

Location in appendix	Section IV
Are inactive ingredients within IIG limits?	Yes
If NO, list ingredients outside of limits	
If a tablet, is the product scored?	N/A
If yes, which strengths are scored?	
Is scoring of RLD the same as test?	
Is the formulation acceptable?	Yes
If not acceptable, why?	

F. In Vitro Dissolution

N/A

G. Waiver Request(s)

Strengths for which waivers are requested	5 mg/5 mL
Regulation cited	21 CFR 320.22 (c)
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	Yes
If not then why?	N/A

H. Deficiency Comments

None

I. Recommendations

The Division of Bioequivalence agrees that the information submitted by Outlook Pharmaceuticals demonstrates that dextroamphetamine sulfate oral solution, 5 mg/5 mL, falls under 21 CFR 320.22(c). A waiver of in vivo bioequivalence study requirements for the test product is granted.

IV. Appendix

Formulation of the test product is provided below.
(Formulation from Section 3.2.P.3 Exhibit Batch formula)

Component	Reference	Pharmaceutical Function	Per mL	% (w/v)
Dextroamphetamine Sulfate, USP	USP	Active ingredient	1.00 mg	0.1
Sorbitol Solution*	USP	(b) (4)		
Saccharin Sodium	USP			
Citric acid, anhydrous	USP			
Sodium citrate	USP			
Benzoic acid	USP			
Bubble Gum Flavor**	----			
Purified water	USP			

* Calculation of % (w/v) sorbitol solution in the formulation is provided below:

Sorbitol Solution, USP is (b) (4) .

(b) (4)

The components and composition of artificial bubble gum flavor is provided in telephone amendment dated July 7, 2006.

** The test formulation contains (b) (4) Bubble Gum Flavor. As per the Chemistry Review (V:\FIRMSNZ\OUTLOOK PHARMACEUTICALS\LTRS&REV\ 40776N01 RSB.doc), the flavoring agent is comprised of (b) (4) . Inactive ingredients are acceptable per IIG. This flavor is in full compliance with 21 CFR 5 101.22.(a) (1) and (3).

As per the Chemistry Review, the components of Artificial Bubble Flavor are as follows:

(b) (4)

Formulation of Dexedrine® Elixir (From NDA 83-902, 2/3/1972).

Components*	mg/5 mL	% (w/v)
Dextroamphetamine Sulfate, USP	5.0	0.10
[redacted] (b) (4)		

Comments

1. The route of administration, dosage form, and strength of the test product are the same as those of the RLD.

2. It is noted that the excipients in the test product are not based on those provided in the labeling of the RLD, Dexedrine®. The test product does not contain alcohol in the formulation.

3. The [redacted] (b) (4) in the test product is sorbitol solution, present at a concentration of [redacted] (b) (4) (w/v). An FDA study has shown that when the sorbitol concentration exceeded 12.5% (w/v) in ranitidine oral solution, ranitidine bioavailability was reduced (See Attachment in Section V).

   It is noted that the reviewer conducted a search on PubMed and did not find any scientific literature that studied effects of sorbitol on bioavailability of dextroamphetamine.

4. All inactive ingredients used in the solution formulation are within the listed levels for oral route of administration products in the Inactive Ingredient Guide (IIG).

5. The firm meets the criteria for a waiver of the in vivo bioequivalence study requirements for its test product per 21 CFR 320.22(c).

V. Attachment

Effect of Sorbitol on Bioequivalence of Ranitidine Oral Solutions

Arthur B. Straughn[1], Nakissa Sadrieh[2], Charles R. Yates[1], Bernd Meibohm[1], Mei-Ling Chen[2] and Ajaz Hussain[2]

[1] Department of Pharmaceutical Sciences, College of Pharmacy, University of Tennessee, Room 5P Crowe Bldg, 874 Union Ave., Memphis, TN 38163.

[2] Office of Pharmaceutical Science, CDER/FDA, 5515 Security Lane, Rockville MD, 20852.

Formulation excipients may affect the bioavailability of drugs. In a previous study in normal volunteers, we showed that 5 gm sorbitol significantly reduced the bioavailability of ranitidine relative to the same ranitidine dose administered with 5 gm of sucrose. The present study describes a four-way crossover in 16 normal male and female volunteers, evaluating the minimal amount of sorbitol required to affect the bioequivalence outcome from an oral solution of ranitidine. Each subject randomly received at weekly intervals one of each of the following solutions:

Tx 1 = 150 mg Ranitidine as HCl and 5 gm Sorbitol in 10 mL aqueous solution
Tx 2 = 150 mg Ranitidine as HCl and 2.5 gm Sorbitol in 10 mL aqueous solution
Tx 3 = 150 mg Ranitidine as HCl and 1.25 gm Sorbitol in 10 mL aqueous solution
Tx 4 = 150 mg Ranitidine as HCl in 10 mL aqueous solution

All doses were administered in the morning after an overnight fast, followed immediately with 240 mL room temperature water. Seven mL blood samples were collected into heparin Vacutainers pre-dose and then at 0.33, 0.67, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10 and 12 hours post dose. Blood was processed and plasma stored at –70c until assayed by a validated HPLC method with UV detection.

Parameter	**Tx 1**	**Tx 2**	**Tx 3**	**Tx 4**
Sorbitol amount (gm)	5	2.5	1.25	0
Tmax (hrs)	2.37	3.04	3.22	3.00
Geo Mean Cmax (ng/mL)	238	362	469	490
Geo Mean AUC last (ng*hr/mL)	1346	1930	2439	2526
Geo Mean AUC inf (ng*hr/mL)	1475	2061	2577	2678
T ½ (hrs)	2.97	2.59	2.39	2.50
Ratio Relative to TX 4 (90% CI)				
Cmax	0.48(0.42-0.57)	0.74(0.64-0.86)	0.96(0.82-1.11)	-----
AUC last	0.53(0.47-0.60)	0.76(0.68-0.87)	0.97(0.85-1.09)	-----
AUC inf	0.55(0.49-0.62)	0.77(0.68-0.83)	0.96(0.85-1.09)	-----

Based on the results of this study in normal volunteers, bioequivalence of an oral solution of ranitidine is not affected by the presence of sorbitol at levels less than or equal to 1.25 gm.

This work conducted under: DHHS Contract FDA 223-02-3004

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-776

APPLICANT: Outlook Pharmaceuticals, Inc.

DRUG PRODUCT: Dextroamphetamine Sulfate Oral Solution
5 mg/5 mL

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

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA: 40-776

1.	**Waiver**	Strength:	5 mg/5 mL
	(WAI)	Outcome:	**AC**
	Submission Date(s)	4/28/2006	

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Devvrat Patel
7/5/2007 09:36:12 AM
BIOPHARMACEUTICS

Kuldeep R. Dhariwal
7/5/2007 10:00:25 AM
BIOPHARMACEUTICS

Dale Conner
7/5/2007 10:10:43 AM
BIOPHARMACEUTICS

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-776

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Mikart

April 28, 2006

505(j)(2)(A) O.K. 12 July 2006

40-776

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: Dextroamphetamine Sulfate Oral Solution, 5mg/5mL

ABBREVIATED NEW DRUG APPLICATION

RECEIVED
MAY 0 1 2006
OGD / CDER

Dear Sir/Madam:

On behalf of Outlook Pharmaceuticals, Inc. of Cincinnati, Ohio, Mikart, Inc. herein submits an abbreviated new drug application (ANDA) for Dextroamphetamine Sulfate Oral Solution, pursuant to section 505 (j) of the Federal Food, Drug and Cosmetics Act. A copy of Outlook Pharmaceuticals' letter of authorization follows this letter in Module 1, section 1.3.1.

This ANDA refers to the previously approved listed drug Dexedrine® Elixir, 5mg/5mL, Application No. 83-902, held by GlaxoSmithKline. It is listed in the electronic Orange Book, *Approved Drug Products with Therapeutic Equivalence Evaluations*, 25th Edition as a Discontinued Drug. Lachman Consulting filed a citizen's petition (Docket 2006P-0125/CP1) on March 17, 2006 requesting the agency make a determination whether the listed drug Dexedrine® 5mg/5mL Elixir was removed from the market for reasons of safety and efficacy; a copy of the petition and the agency's acknowledgement letter is included in Module 1, section 1.4.3.

There are no un-expired patents or un-expired exclusivity for this product.

A bioequivalency/bioavailability study was not conducted for the proposed drug product; as a solution, the results are considered self-evident. Mikart is requesting a waiver of in-vivo bioequivalence studies for Dextroamphetamine Sulfate Oral Solution 5mg/5mL in accordance with 21 CFR320.22.

This application provides for the manufacture, processing and packaging of Dextroamphetamine Sulfate Oral Solution, 5mg/5mL at Mikart, Inc., Atlanta, GA. The release testing and stability studies are also performed by Mikart, Inc.

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Dextroamphetamine Sulfate Oral Solution, 5mg/5mL is stable; a two (2) year expiration dating period is requested. The proposed two year expiration dating of this product is supported by 30, 60 and 90 day accelerated stability data (40° C ±2° C/ 75 ± 5% relative humidity) and 3 month controlled room temperature stability data (25°C ± 2°C, 60 ± 5% relative humidity).

The conditions of use (except as noted), active ingredients, route of administration, strength, dosage form, dosage and administration, marketing status and labeling (except as annotated) for Dextroamphetamine Sulfate Oral Solution, 5mg/5mL are the same as those of the listed drug. This abbreviated new drug application refers to approved labeling for Dexedrine® (Dextroamphetamine Sulfate) 5mg/5mL Elixir, Application No. 83-902. Dexedrine® Elixir was also indicated for exogenous obesity; however that indication has been removed from the proposed drug product.

Mikart, Inc. hereby commits to resolve any issues identified in the method validation process after approval.

The USP monograph for Dextroamphetamine Sulfate Oral Solution has been removed from the current USP (USP29), but was included in USP28 when the registration/exhibit batch was manufactured for this application. Please note the exhibit and scale-up batch documentation includes the "USP" designation. The specifications meet the USP requirements; however, the labeling of future commercial batches will include this designation only if the monograph is reintroduced.

This ANDA, in CTD format, is submitted in five binders as follows:

Module 1 Administrative Information
Module 2 CTD Summaries
Module 3 Quality: Drug Substance
Module 3 Quality: Drug Product
Module 3 Quality: Regional Information

Outlook Pharmaceuticals intends to market the proposed drug product in one commercial package of 16-ounce bottles.

This submission includes electronic Labeling and Bioavailability/Bioequivalence information on one CDROM with an approximate size of 1.0 megabytes. This CDROM is virus free and has been checked for viruses using Norton Antivirus software.

Mikart, Inc. certifies that true copies of the technical sections described in 21 CFR 314.94 (a) (9) of this submission have been provided to the Cincinnati and Atlanta District Offices of the Food and Drug Administration.

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Thank you for your attention to the review of this material. If you have any questions or concerns regarding this submission, please contact Lisa Apolis, Regulatory Submissions, or me at (404) 351- 4510.

Sincerely,

Pieter J. Groenewoud
Vice President, R&D

PJG:la

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Mikart

July 07, 2006

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 40-776 TELEPHONE AMENDMENT
Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL

Dear Sir/Madam:

Reference is made to the Office of Generic Drug's June 29, 2006 telephone communication related to the subject application. Reference is also made to Mikart, Inc's abbreviated new drug application dated April 28, 2006.

Mr. Iain Margand, with the Office of Generic Drugs, presented five observations related to the Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL. Mikart, Inc. herein submits a complete and full response to all items listed in the telephone amendment. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

Mikart, Inc. certifies that a true copy of the technical sections described in 21 CFR 314.94(a)(9) of this submission has been provided to the Atlanta and Cincinnati District Offices of the Food and Drug Administration.

Thank you for your attention to the review of this information. If you have any questions or concerns regarding this submission, please contact Lisa Apolis, Manager of Regulatory Submissions at (404) 351-4510.

Sincerely,

Pieter Groenewoud
Vice-President, R&D

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

****For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www.fda.gov/cder/regulatory/ersr/ectd.htm**
*****For a Comprehensive Table of Contents Headings and Hierarchy please go to: http://www.fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf**
** For more CTD and eCTD informational links see the final page of the ANDA Checklist
*** A model Quality Overall Summary for an immediate release table and an extended release capsule can be found on the OGD webpage **http://www.fda.gov/cder/ogd/** ***

ANDA #: 40-776 **FIRM NAME:** OUTLOOK PHARMACEUTICALS

PIV: NO **Electronic or Paper Submission:** PAPER

RELATED APPLICATION(S): SEE 83-902 FROM GLAXO SMITH KLINE FOR DEXTROAMPHETAMINE SULFATE ORAL SOLUTION, 5 MG/5 ML (AP 2/26/76) (DISC SECTION)

First Generic Product Received? NO

Bio Assignments:		**Micro Review (No)**
☒ **BPH**	☐ **BCE**	☐
☐ **BST**	☐ **BDI**	

DRUG NAME: DEXTROAMPHETAMINE SULFATE
DOSAGE FORM: ORAL SOLUTION , 5 MG/5 ML

Random Queue: 7
Chem Team Leader: M. Scott Furness PM: Yoon Kong Labeling Reviewer: Koung Lee

Letter Date: APRIL 28, 2006 **Received Date:** MAY 01, 2006

Comments: EC- 1 YES **On Cards:** YES
Therapeutic Code: 2020500 ANOREXIGENIC AGENTS

Archival copy: PAPER **Sections** I
Review copy: YES E-Media Disposition: YES SENT TO EDR
Not applicable to electronic sections

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Iain Margand	**Recommendation:**
Date 7/11/06	☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date:	**Date:** 12 July 2006

ADDITIONAL COMMENTS REGARDING THE ANDA:

6/29/06:Requested unit composition for Drug Product (3.2.P.1)
Requested component/composition for Bubble Gum Flavor.
Requested Letter of Authorization for U.S. agent to act on behalf of ANDA applicant.
Requested revision of Bio Waiver Request to cite correct regulation. Should be 21CFR 320.22(b)(3).
Requested revised component/composition formulation for Drug Product. Water is listed in executed batch records to make drug product, but is not listed in the drug product formulation in the component/composition section.
Requested test specifications and COA's for water used in drug product exhibit batch.

7/11/06: Received requested information. Application delayed by Bubble Gum Flavor formulation.
Contact: Lisa Apolis 404-351-4510

MODULE 1
ADMINISTRATIVE

		ACCEPTABLE
1.1	**1.1.2** **Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) RX YES	☒
1.2	**Cover Letter** Dated: APRIL 28, 2006	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** YES **(N/A for E-Submissions)**	☒
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature) YES	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) or Disclosure Statement (Form FDA 3455) NO - no bio studies performed	☐
1.3.5	**1.3.5.1** **Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations None **1.3.5.2** **Patent Certification** 1. Patent number(s) N/A 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☒ PII ☐ PIII ☐ PIV ☐ No Relevant Patents ☐ 3. Expiration of Patent(s): NA a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: YES no exclusivities	☒

1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient Y b. Type III DMF authorization letter(s) for container closure Y 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) Y	☒
1.12.11	**Basis for Submission** NDA# : 83-902 Ref Listed Drug: DEXEDRINE Firm: GLAXO SMITH KLINE ANDA suitability petition required? YES 2006P-0125/CP1 LETTER DATED 3/17/06 If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1 **No**	☒

MODULE 1 (Continued)
ADMINISTRATIVE

		ACCEPTABLE
1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same, except have removed obesity 2. Active ingredients Sextroamphetamine Sulfate 3. Inactive ingredients N/A 4. Route of administration Oral 5. Dosage Form Oral Solution 6. Strength 5 mg/mL	☒
1.12.14	**Environmental Impact Analysis Statement**	☒
1.12.15	**Request for Waiver 21 CFR 320.22(b)(3)** Request for Waiver of In-Vivo BA/BE Study(ies): Paper, YES	☒
1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) Y **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained Y **1.14.1.3** 1 package insert (content of labeling) submitted electronically Y ***Was a proprietary name request submitted? No (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained Y **1.14.3.3** 1 RLD label and 1 RLD container label Y	☒

MODULE 2
SUMMARIES

ACCEPTABLE

2.3	**Quality Overall Summary** **E-Submission: _____PDF (archive) ____ Word Processed e.g., MS Word** A model Quality Overall Summary for an immediate release table and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/ **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient)** Y **2.3.S.1** **General Information** **2.3.S.2** **Manufacture** **2.3.S.3** **Characterization** **2.3.S.4** **Control of Drug Substance** **2.3.S.5** **Reference Standards or Materials** **2.3.S.6** **Container Closure System** **2.3.S.7** **Stability** **2.3.P** **Drug Product** Y **2.3.P.1** **Description and Composition of the Drug Product** **2.3.P.2** **Pharmaceutical Development** **2.3.P.2.1** **Components of the Drug Product** **2.3.P.2.1.1** **Drug Substance** **2.3.P.2.1.2** **Excipients** **2.3.P.2.2** **Drug Product** **2.3.P.2.3** **Manufacturing Process Development** **2.3.P.2.4** **Container Closure System** **2.3.P.3** **Manufacture** **2.3.P.4** **Control of Excipients** **2.3.P.5** **Control of Drug Product** **2.3.P.6** **Reference Standards or Materials** **2.3.P.7** **Container Closure System** **2.3.P.8** **Stability**	☒

2.7	**Clinical Summary (Bioequivalence)** N/A **E-Submission: _____PDF (archive) ____ Word Processed e.g., MS Word** **2.7.1** **Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1** **Background and Overview** **2.7.1.2** **Summary of Results of Individual Studies** **2.7.1.3** **Comparison and Analyses of Results Across Studies** **2.7.1.4** **Appendix**	☐

MODULE 3

3.2.S DRUG SUBSTANCE

ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1** **Nomenclature** Y **3.2.S.1.2** **Structure** Y **3.2.S.1.3** **General Properties** Y	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Addresses of bulk manufacturers Y 2. Manufacturing Responsibilities Y 3. Type II DMF number for API # (b) (4) 4. CFN or FEI numbers	☒
3.2.S.3	**Characterization**	☒

3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1** **Specification** Testing specifications and data from drug substance manufacturer(s) Y **3.2.S.4.2** **Analytical Procedures** Y **3.2.S.4.3** **Validation of Analytical Procedures** **1.** Spectra and chromatograms for reference standards and test samples Y 2. Samples-Statement of Availability and Identification of: a. Drug Substance see section 3.2.R.3.S b. Same lot number(s) **3.2.S.4.4** **Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) Y 2. Applicant certificate of analysis Y **3.2.S.4.5** **Justification of Specification** Y	☒
3.2.S.5	**Reference Standards or Materials**	☒
3.2.S.6	**Container Closure Systems**	☒
3.2.S.7	**Stability**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1	**Description and Composition of the Drug Product** 1) Unit composition Y 2) Inactive ingredients are appropriate per IIG – Inactive ingredients are acceptable per IIG and COMIS	☒
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report	☒
3.2.P.3	**Manufacture** **3.2.P.3.1** **Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) YES 2. CGMP Certification: YES - see section 1.3.3 3. Function or Responsibility YES see section 1.3.3 4. CFN or FEI numbers **3.2.P.3.2** **Batch Formula** Batch Formulation Y **3.2.P.3.3** **Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process Y 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) 3. If sterile product: Aseptic fill / Terminal sterilization N/A 4. Reprocessing Statement Y **3.2.P.3.4** **Controls of Critical Steps and Intermediates** Y **3.2.P.3.5** **Process Validation and/or Evaluation** 1. Microbiological sterilization validation N/A 2. Filter validation (if aseptic fill) N/A	☒
3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified Y **3.2.P.4.1** **Specifications** 1. Testing specifications (including identification and characterization) Y 2. Suppliers' COA (specifications and test results) Y **3.2.P.4.2** **Analytical Procedures** Y **3.2.P.4.3** **Validation of Analytical Procedures** Y **3.2.P.4.4** **Justification of Sepcifications** Applicant COA Y	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1** **Specification(s)** Y **3.2.P.5.2** **Analytical Procedures** Y **3.2.P.5.3** **Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form see section 3.2.R.3.S 2. Same lot numbers **3.2.P.5.4** **Batch Analysis** Certificate of Analysis for Finished Dosage Form Y Lot # J050527 **3.2.P.5.5** **Characterization of Impurities** Y **3.2.P.5.6** **Justification of Specifications** Y	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) Y 2. Components Specification and Test Data Y 3. Packaging Configuration and Sizes 16 ounce plastic bottle 4. Container/Closure Testing Y 5. Source of supply and suppliers address Y	☒
3.2.P.8	**3.2.P.8.1** **Stability (Finished Dosage Form)** 1. Stability Protocol submitted Y 2. Expiration Dating Period 2 years **3.2.P.8.2** **Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments Y **3.2.P.8.3** **Stability Data** 1. 3 month accelerated stability data Y 2. Batch numbers on stability records the same as the test batch lot # J050527	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S** N/A **Executed Batch Records for drug substance (if available)** **3.2.R.2.S** **Comparability Protocols** **3.2.R.3.S** **Methods Validation Package** NO Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☐

MODULE 3
3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation J050527 Theoretical Yield (b) (4) Actual Yield Packaged Yield bottles **3.2.R.1.P.2** **Information on Components** Y **3.2.R.2.P** **Comparability Protocols** N/A **3.2.R.3.P** **Methods Validation Package Y** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

MODULE 5
CLINICAL STUDY REPORTS N/A

ACCEPTABLE

5.2	**Tabular Listing of Clinical Studies**	☐
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers of Products used in BE Study(ies):** **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐
	5.3.1.2 **Comparative BA/BE Study Reports** Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** In-Vitro Dissolution: **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** Bioanalytical validation report **5.3.7** **Case Report Forms and Individual Patient Listing**	☐
5.4	**Literature References**	
	Possible Study Types:	

Study Type	**IN-VIVO PK STUDY(IES)** (i.e., fasting/fed/sprinkle) NA 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted: YES SENT TO EDR 3. In-Vitro Dissolution: NO	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐
Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% or 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** NO 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 4/18/2006 C. Bina

****CTD and eCTD Informational Links**

Organization of the CTD
http://www.fda.gov/cder/guidance/4539O.PDF

eCTD Submissions
http://www.fda.gov/cder/guidance/6766fnl.pdf

Drug Substance
http://www.fda.gov/cder/guidance/3969DFT.pdf

Drug Product
http://www.fda.gov/cder/guidance/1215dft.pdf

Pharmaceutical Development
http://www.fda.gov/cder/guidance/6672dft.pdf

CTD-Efficacy
http://www.fda.gov/cder/guidance/4539E.pdf

CTD-Quality
http://www.fda.gov/cder/guidance/4539Q.PDF

ANDA 40-776 Final Check List for Branch Chief

- ✓ 1) Check letter date and stamp date of ANDA vs. drafted letter.
- ✓ 2) Check for any NC arriving post stamp date but prior to Reg. Review.
- ✓ 3) Check for gross errors in letter.
- ✓ 4) Check that correct letter format is used. (PIV vs. Other acknowledgment)
- ✓ 5) Check address and contact person on letter vs. 356h.
- ✓ 6) Check for any t-cons and verify date and correspondence date.
- ✓ 7) Check Patent Certification information in entered in COMIS (by Eda) vs. Actual certification. If multiple patent certifications, should be based on PIV if applicable or latest expiring patent.
- ✓ 8) Check for any comments or problems raised by reviewer on Check List.
- ✓ 9) If first generic, copy BE review and file.
- ✓ 10) Sign Check List.
- ✓ 11) Check electronic Orange Book to verify current patent information and correct RLD.
- N/A 12) Check for MOU patents
- ✓ 13) Review 356h. Check NDA number and RLD for correct reference. If proprietary name proposed, notify Labeling reviewer.
- ✓ 14) Review Basis for Submission. 2006P-0125/CP1 C.P for S/E 83-902
- ✓ 15) Review Patent Certifications and Exclusivity Statement. (If an expiration of an exclusivity has occurred make a note to the Labeling reviewer.
- ✓ 16) Review Comparison between Generic Drug and RLD for: condition of use, active ingredients, route of administration, dosage form and strength. Check Components and Composition.
- ✓ 17) Sign cover letter 505 (j)(2)(A) OK, date, and full signature.
- ✓ 18) Pull USP information. (USP ____yes ✓ no)
- ✓ 19) Final Grammar review on letter.
- ✓ 20) Verify information in OGD Patent Tracking System.
- ✓ 21) EES slip.
- ✓ 22) Document in record book.

Signature Martin H Gru date 12 July 2006

2.1

ANDA 40-776

Mikart, Inc.
U.S. Agent for: Outlook Pharmaceuticals, Inc.
Attention: Pieter Groenewoud
1750 Chattahoochee Avenue
Atlanta, GA 30318

Dear Sir:

JUL 13 2006

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to the telephone conversation dated June 29, 2006 and your correspondence dated July 7, 2006.

NAME OF DRUG: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

DATE OF APPLICATION: April 28, 2006

DATE (RECEIVED) ACCEPTABLE FOR FILING: May 1, 2006

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Yoon Kong
Project Manager
(301)827-5791

Sincerely yours,

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 40-776
cc: DUP/Jackets
HFD-600/Division File
Field Copy
HFD-92
Endorsement:
HFD-613/MShimer, Chief, RSB _____ date 12 July 06
HFD-613/IMargand, CSO _____ date 7/11/06
Word File V:\Firmsnz\Outlook\Ltrs&rev\40776.ack
F/T 7/11/06
ANDA Acknowledgment Letter!

MINOR AMENDMENT

ANDA 40-776

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

SEP 28 2006

APPLICANT: Mikart Inc.
U.S. Agent for Outlook Pharmaceuticals, Inc.

TEL: 404-351-4510 ext.301

FAX: 404-352-0451

ATTN: Pieter Groenewoud, Vice President, R&D

PROJECT MANAGER: (301) 827-5791

FROM: Yoon Kong

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated April 28, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (3 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

UC 9/27/06

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

SEP 28 2006

ANDA: 40-776 APPLICANT: Outlook Pharmaceuticals, Inc.

DRUG PRODUCT: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL.

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. (b) (4)
2.
3.
4.
5.
6.
7.
8.
9.

10. (b) (4)

11.

12.

13.

14.

15.

16.

17.

18.

19.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate covers.

A satisfactory CGMP compliance evaluation for the firms referenced in the ANDA is required for approval. We have requested an evaluation from the Division of Manufacturing and Product Quality.

Sincerely yours,

for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Mikart

RECEIVED
MAR 26 2007
OGD / CDER

ORIGINAL

March 23, 2007

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ORIG AMENDMENT
3/26/07

RE: ANDA 40-776 MINOR AMENDMENT
Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL

Dear Sir/Madam:

Reference is made to the Office of Generic Drug's chemistry deficiency facsimile dated September 28, 2006 related to the subject application. Reference is also made to Outlook Pharmaceutical's abbreviated new drug application dated April 28, 2006 and telephone amendment dated July 7, 2006.

Ms. Yoon Kong, Project Manager with the Office of Generic Drugs, presented nineteen observations related to the Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL. As the regulatory agent for Outlook Pharmaceuticals, Inc., Mikart, Inc. herein submits a complete and full response to all items listed in the amendment. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

Mikart, Inc. certifies that a true copy of the technical sections described in 21 CFR 314.94(a)(9) of this submission has been provided to the Cincinnati District Office of the Food and Drug Administration.

Thank you for your attention to the review of this information. If you have any questions or concerns regarding this submission, please contact me at (404) 351-4510.

Sincerely,

Lisa Apolis

Lisa Apolis
Manager, Regulatory Submissions

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Mikart

ORIG AMENDMENT

N

May 22, 2007

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 40-776 TELEPHONE AMENDMENT
Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL

Dear Sir/Madam:

Reference is made to the Office of Generic Drug's chemistry deficiency telephone amendment on May 17, 2007 related to the subject application. Reference is also made to Outlook Pharmaceutical's abbreviated new drug application dated April 28, 2006, telephone amendment dated July 7, 2006, and minor amendment dated March 23, 2007.

Mr. Scott Furness, OGD CMC Team Leader with the Office of Generic Drugs, presented three observations related to the Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL. As the regulatory agent for Outlook Pharmaceuticals, Inc., Mikart, Inc. herein submits a complete and full response to all items listed in the amendment. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

Thank you for your attention to the review of this information. If you have any questions or concerns regarding this submission, please contact me at (404) 351-4510.

Sincerely,

Lisa Apolis

Lisa Apolis
Manager, Regulatory Submissions

RECEIVED
MAY 23 2007
OGD

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Mikart

ORIG AMENDMENT

N/AM

June 1, 2007

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 40-776 TELEPHONE AMENDMENT
Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL

Dear Sir/Madam:

Reference is made to the Office of Generic Drug's chemistry deficiency telephone amendment on May 23, 2007 related to the subject application. Reference is also made to Outlook Pharmaceutical's abbreviated new drug application dated April 28, 2006, telephone amendment dated July 7, 2006, minor amendment dated March 23, 2007 and telephone amendment dated May 22, 2007.

Mr. Scott Furness, OGD CMC Team Leader with the Office of Generic Drugs, presented one observation related to the Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL. As the regulatory agent for Outlook Pharmaceuticals, Inc., Mikart, Inc. herein submits a complete and full response to all items listed in the amendment. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

Thank you for your attention to the review of this information. If you have any questions or concerns regarding this submission, please contact me at (404) 351-4510.

Sincerely,

Lisa Apolis

Lisa Apolis
Manager, Regulatory Submissions

RECEIVED
JUN 4 2007
OGD

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Telephone Fax

ANDA 40-776

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8981

TO: Outlook Pharmaceuticals Inc. TEL: 404-351-4510

ATTN: Pieter Groenewoud FAX: 404-352-0351

FROM: Koung Lee

:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for _Dextroamphetamine Sulfate Oral Solution_.

Pages (including cover): _4___

SPECIAL INSTRUCTIONS:

Labeling Comments

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-776 Date of Submission: April 28, 2006

Applicant's Name: Outlook Pharmaceuticals, Inc.

Established Name: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

Labeling Deficiencies:

1. CONTAINER (473 mL)

   a. Delete "(b) (4)

   b. Increase the expression of strength.

   c. Revise the storage temperature statement to read "Store at 20^0 to 25^0C (68^0 to 77^0F)[see USP controlled room temperature]".

   d. Please confirm whether the (b) (4) printed liner with red highlighted letter satisfies 21 CFR 1302.06 (Sealing of controlled substances).

   e. Relocate the bottom statement on the principal display panel to the side panel and revise to read "Each 5 mL contains dextroamphetamine sulfate, 5 mg."

   f. Include the statement "PHARMACIST: Dispense Medication Guide with the Drug Product".

2. INSERT

   a. New labeling was approved for Dexedrine Spansule Sustained-Release Capsules on May 1, 2007. Prior to the withdrawal of Dexedrine Elixir from the market, it shared the insert labeling with Dexedrine Spansule and Dexedrine Tablets. The new safety information approved for Dexedrine appears to apply for all formulations including the oral solution. Please review the approved labeling for Dexedrine Spansule available on the Drugs@FDA website and revise accordingly.

   b. CLINICAL PHARMACOLOGY

      Revise the first paragraph to read as follows:

      "Ingestion of 10 mg of dextroamphetamine sulfate in oral solution form by healthy volunteers produced an average peak dextroamphetamine blood level of 33.2 ng/mL. The half-life was 11.75 hours. The average urinary recovery was 38% in 48 hours."

3. MEDICATION GUIDE

   a. Dexedrine Spansule and Tablet are approved with a Medication Guide. The medication guide should also be made available for proposed dextroamphetamine oral solution.

   b. Please indicate the number medication guides you intend to include for each bottle and how they will be made available.

Please revise your labeling as described above and submit electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Lillie Golson
7/3/2007 12:25:29 PM
Lillie Golson for Wm. Peter Rickman

Mikart

ORIG AMENDMEN

September 14, 2007

N000/AF

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 40-776 LABELING AMENDMENT
Dextroamphetamine Sulfate Oral Solution 5 mg/5 mL

Dear Sir/Madam:

Reference is made to Mikart, Inc.'s abbreviated new drug application dated April 28, 2006. Reference is also made to correspondence dated July 7, 2006 and chemistry amendments dated March 23, 2007, May 22, 2007 and June 1, 2006.

The Division of Labeling and Program Support, Labeling Review Branch, listed three observations related to the final print labeling for Dextroamphetamine Sulfate Oral Solution 5 mg/5 mL Mikart, Inc. herein submits a complete and full response to all items listed in the amendment. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

This submission also includes electronic labeling information in PDF and SPL format on one CDROM with an approximate size of 989KB. This CDROM is virus free and has been checked for viruses using Norton Antivirus software.

Thank you for your attention to the review of this material. If you have any questions or concerns regarding this submission, please contact me at (404) 351- 4510.

Sincerely,

Pieter Groenewoud
Vice President, R&D

RECEIVED

SEP 17 2007

OGD

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Telephone Fax

ANDA 40-776

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8981

TO: Outlook Pharmaceuticals Inc. TEL: 404-351-4510

ATTN: Pieter Groenewoud FAX: 404-352-0451

FROM: Koung Lee

:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for _Dextroamphetamine Sulfate Oral Solution_.

Pages (including cover): _5___

SPECIAL INSTRUCTIONS:

Labeling Comments

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-776 Date of Submission: September 14, 2007

Applicant's Name: Outlook Pharmaceuticals, Inc.

Established Name: Dextroamphetamine Sulfate Oral Solution, 5 mg/5 mL

Labeling Deficiencies:

1. CONTAINER (473 mL)

   a. Further increase the prominence of the expression of strength.

   b. Revise the storage temperature statement to read "Store at 20° - 25°C (68° - 77°F) (See USP Controlled Room Temperature)".

2. INSERT

   a. BOXED WARNING

      Correct the spelling of "THERAPEUTIC" in the last sentence of the first paragraph.

   b. DESCRIPTION

      i. The inactive ingredients do not need to be capitalized.

      ii. Add "hydrous" at the end of "sodium citrate".

   c. CLINICAL PHARMACOLOGY

      Relocate the first paragraph to replace the first paragraph in the "Pharmacokinetics" subsection.

   d. INDICATIONS AND USAGE

      Replace "emotionally" with "emotional" in the first sentence of the "Attention Deficit Disorder with Hyperactivity" subsection.

   e. WARNINGS

      i. Add "s" at the end of "*Adolescent*" in the subsection heading "Sudden Death in…Heart Problems: *Children and Adolescents*".

      ii. In the first sentence under "Assessing Cardiovascular Status in…with Stimulant Medications:" add an "s" at the end of "medication" in the first sentence.

      iii. In the penultimate sentence in the "Long-Term Suppression of Growth" subsection, replace "or" with "no".

   f. PRECAUTIONS

      i. Add the following to appear as the second paragraph in the "Information for Patients" subsection:

         Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with dextroamphetamine and should counsel them in its appropriate use. A patient Medication Guide is available for dextroamphetamine sulfate. The prescriber or health professional should instruct patients, their families, and their caregivers to

read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

ii. In the second sentence of the "*Alkalinizing agents*" subsection, replace "alkalizing" with "alkalinizing".

iii. Carcinogenesis/Mutagenesis

Delete "(b) (4)".

iv. Pregnancy-Teratogenic Effects

Delete "(b) (4)" in the first and last sentence.

v. Pediatric Use

In the second sentence of the third paragraph, delete the "s" at the end of "evaluations".

g. DOSAGE AND ADMINISTRATION (Narcolepsy)

i. Revise the first sentence to read "Usual dose is 5 mg to 60 mg per day…"

ii. In the second sentence of the second paragraph, revise to read "…aged 6 to 12 is 5 mg daily…"

iii. Add the following at the end of the second paragraph:

"Give first dose on awakening; additional doses (1 or 2) at intervals of 4 to 6 hours."

h. HOW SUPPLIED

Revise the storage temperature statement to read "Store at 20^{o} - 25^{o}C (68^{o} - 77^{o}F) (See USP Controlled Room Temperature)".

3. MEDICATION GUIDE

a. Heart-related problems:

Revise the third paragraph to read "Your doctor should check your or your child's blood pressure…"

b. What is Dextroamphetamine Sulfate Oral Solution

Delete the second sentence in the first pagraph.

c. Who should not take Dextroamphetamine Sulfate Oral Soution?

Delete the fourth bulleted statement "(b) (4)".

d. How should Dextroamphetamine Sulfate Oral Solution be taken?

Revise the second paragrah to read as follows:

Dextroamphetamine Sulfate Oral Solution is usually taken two to three times a day. The first dose is usually taken in the morning. One or two more doses may be taken during the day, 4 to 6 hours apart.

Please revise your labeling as described above and submit electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Lillie Golson
10/15/2007 04:16:24 PM
Lillie Golson for Wm. Peter Rickman

Mikart

November 14, 2007

ORIG AMENDMENT

N/AF

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 40-776 LABELING AMENDMENT
Dextroamphetamine Sulfate Oral Solution 5 mg/5 mL

Dear Sir/Madam:

Reference is made to Outlook Pharmaceutical's abbreviated new drug application dated April 28, 2006. Reference is also made to correspondence dated July 7, 2006, labeling amendment September 14, 2007 and chemistry amendments dated March 23, 2007, May 22, 2007 and June 1, 2007.

The Division of Labeling and Program Support, Labeling Review Branch, listed three observations related to the final print labeling for Dextroamphetamine Sulfate Oral Solution 5 mg/5 mL as the regulatory agent for Outlook Pharmaceuticals, Inc., Mikart, Inc. herein submits a complete and full response to all items listed in the amendment. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

This submission also includes electronic labeling information in PDF and SPL format on one CDROM with an approximate size of 993KB. This CDROM is virus free and has been checked for viruses using Norton Antivirus software.

Thank you for your attention to the review of this material. If you have any questions or concerns regarding this submission, please contact me at (404) 351- 4510.

Sincerely,

Pieter Groenewoud by Lapoli

Pieter Groenewoud
Vice President, R&D

RECEIVED

NOV 15 2007

OGD

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Mikart

ORIG AMENDMENT

N/A

January 16, 2008

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 40-776 TELEPHONE AMENDMENT
Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL

Dear Sir/Madam:

Reference is made to the Office of Generic Drug's telephone conversation on January 14, 2008, related to the subject application. Reference is also made to Outlook Pharmaceutical's abbreviated new drug application dated April 28, 2006, telephone amendments dated July 7, 2006, chemistry amendments dated March 23, May 22 and June 1, 2007 and labeling amendments dated September 14 and November 14, 2007.

Ms. Sema Basaran, with the Office of Generic Drugs, presented three observations related to the Dextroamphetamine Sulfate Oral Solution, 5 mg/ 5 mL. As the regulatory agent for Outlook Pharmaceuticals, Inc., Mikart, Inc. herein submits a complete and full response to all items discussed in the conversation. To assist the review of the submission, each Agency comment is printed in bold type followed by the sponsor's point-by-point response.

Thank you for your attention to the review of this information. If you have any questions or concerns regarding this submission, please contact me at (404) 351-4510.

Sincerely,

Lisa Apolis

Lisa Apolis
Director, Regulatory Submissions

RECEIVED

JAN 18 2008

OGD

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

OGD APPROVAL ROUTING SUMMARY

ANDA # 40-776 Applicant Outlook Pharmaceuticals, Inc.
Drug Dextroamphetamine Sulfate Oral Solution Strength(s) 5 mg/5 mL

APPROVAL ☒ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **OTHER** ☐

REVIEWER: **DRAFT Package** **FINAL Package**

1. **Martin Shimer** Date 8 Jan 2008 Date 1/28/08
Chief, Reg. Support Branch Initials MHS Initials rlw
Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92) Pediatric Exclusivity System
RLD = _____ NDA# 83-902
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked N/A
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐ Written request issued ☐
Was applicant sued w/in 45 days: Yes ☐ No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐ Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒
Date of latest Labeling Review/Approval Summary _____
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒
Type of Letter: Full Approval
Comments: The BOS for this ANDA is Dexedrine Oral Elixir which had been marketed under ANDA 83-902. At the time of submission the firm referenced CP 2006P-0125/CP1 requesting that the Agency formally determine that Dexedrine Oral Elixir was not discontinued for S/E reasons. FR Vol 72 No. 151 Dated August 7, 2007 contains the Agency's formal determination that Dexedrine Oral Elixir was not D/C'd for S/E reasons. There are no patent, exclusivity or other regulatory barriers to the issuance of a Full Approval. ANDA is eligible for Full Approval.

2. Project Manager, Theresa Liu Team 7 Date 1/4/08 Date _____
Review Support Branch Initials tcl Initials _____

Original Rec'd date 4/28/06 EER Status Pending ☐ Acceptable ☒ OAI ☐
Date Acceptable for Filing 5/1/06 Date of EER Status 3/15/07
Patent Certification (type) pI Date of Office Bio Review 7/6/07
Date Patent/Exclus.expires Date of Labeling Approv. Sum _____
Citizens' Petition/Legal Case Yes ☐ No ☒ Labeling Acceptable Email Rec'd Yes ☐ No ☐
(If YES, attach email from PM to CP coord) Labeling Acceptable Email filed Yes ☐ No ☐
First Generic Yes ☐ No ☒ Date of Sterility Assur. App. _____
Priority Approval Yes ☐ No ☒ Methods Val. Samples Pending Yes ☐ No ☐
(If yes, prepare Draft Press Release, Email it to Cecelia Parise) MV Commitment Rcd. from Firm Yes ☐ No ☐
Acceptable Bio reviews tabbed Yes ☐ No ☒ Modified-release dosage form: Yes ☐ No ☐
Bio Review Filed in DFS: Yes ☒ No ☐ Interim Dissol. Specs in AP Ltr: Yes ☐
Suitability Petition/Pediatric Waiver Yes ☒
Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐
Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def. /NA Minor issued ☐ Date _____
Comments:

3. Labeling Endorsement
Reviewer: Labeling Team Leader:
Date January 8, 2008 Date 1/8/08
Name/Initials Koung Lee/KL Name/Initials LG

Comments:
Hi Theresa,

From a labeling standpoint, this application is acceptable for approval. Please endorse the AP routing slip on behalf of Koung and me.

Thanks

p.s. I replaced "entitled" with "titled" in sentence referring to the OB.

From: Lee, Koung U
Sent: Tuesday, January 08, 2008 1:44 PM
To: Liu, Theresa
Cc: Golson, Lillie D
Subject: FW: ANDA 40-776

Hi Theresa,

I concur. No changes in the Dexedrine labeling and no changes in the USP.

Koung

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date 1/28/08
OGD Regulatory Counsel, Post-MMA Language Included ☐ Initials rlw/for
Comments:N/A. No patents are listed in the current "Orange Book" for this drug product.

5. Div. Dir./Deputy Dir. Date1/25/08
Chemistry Div. II Initials FF

Comments:Finished product and stability testing revised. (1/16/08 amendment)
CMC OK

6. Frank Holcombe **First Generics Only** Date1/28/08
Assoc. Dir. For Chemistry Initials rlw/for
Comments: (First generic drug review)
N/A. The reference listed drug product, GSK's Dexedrine Elixir, was approved as an ANDA

7. Vacant Date_____
Deputy Dir., DLPS Initials_____
RLD = Dexedrine Elixir 5 mg/5 mL
GlaxoSmithKline ANDA 83-902

Note: The RLD is currently in the "discontinued" section of the "Orange Book". A Federal Register Notice issued on August 7, 2007 finding that GSK's Dexedrine Elixir was not withdrawn from the market for reasons of safety or effectiveness.

8. Peter Rickman Date1/28/08
Director, DLPS Initials rlw/for
Para.IV Patent Cert: Yes☐ No☐;Pending Legal Action: Yes ☐No ☐;Petition: Yes☐ No☐
Comments:Bioequivalence waiver granted under 21 CFR 320.22( ). Drug product is "AA-rated" in the Orange Book". Office-level bio endorsed 7/5/07.

Final-printed labeling (FPL) found acceptable for approval 1/7/08.

CMC found acceptable for approval (Chemistry Review #2) 6/5/07.

OR

8. Robert L. West Date 1/28/08
Deputy Director, OGD Initials RLWest
Para.IV Patent Cert: Yes☐ No☐; Pending Legal Action: Yes☐ No☐; Petition: Yes☐ No☐
Press Release Acceptable ☐
Comments:Acceptable EES dated 3/15/07 (Verified 1/28/08). No "OAI" Alerts noted.

There are no patents or exclusivity listed in the current "Orange Book" for this drug product.

With the issuance of the Federal Regiatrer Notice on August 7, 2007, finding that the reference listed drug product, GSK's Dexedrine Elixir (Oral Solution), was not withdrawn from the market for reasons of safety or effectiveness, this ANDA is recommended for approval.

9. Gary Buehler Date 1/28/08
Director, OGD Initials rlw/for
Comments:
First Generic Approval ☒ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, Theresa Liu Team 7 Date1/29/08
Review Support Branch Initials tcl
_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
11 am Time notified of approval by phone 11 am Time approval letter faxed

FDA Notification:
1/29/08 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
1/29/08 Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

ORANGE BOOK PRINT OFF:

Search results from the "OB_Disc" table for query on "083902."

Active Ingredient:	DEXTROAMPHETAMINE SULFATE
Dosage Form;Route:	ELIXIR; ORAL
Proprietary Name:	DEXEDRINE
Applicant:	GLAXOSMITHKLINE
Strength:	5MG/5ML **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**
Application Number:	083902
Product Number:	001
Approval Date:	Approved Prior to Jan 1, 1982
RX/OTC/DISCN:	DISCN
Patent and Exclusivity Info for this product:	View

Return to Electronic Orange Book Home Page

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 December, 2007
Patent and Generic Drug Product Data Last Updated: January 25, 2008

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Theresa Liu

1/29/2008 09:21:53 AM