CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-248/S-027

APPROVAL LETTER

MAY 3 1 2000

NDA 18-248/S-027

American Pharmaceuticals Partners, Inc.
Attention: Genny Cruz
Senior Regulatory Scientist
2045 North Cornell Avenue
Melrose Park, Il 60160

Dear Ms. Cruz:

Please refer to your supplemental new drug application dated February 29, 2000, received March 8, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytocin Injection, USP (Synthetic).

This "Changes Being Effected in 30 days" supplemental new drug application provides for the following changes to the package insert:

Addition of an impurity statement:

DESCRIPTION section

"This product may contain up to 12.5% decomposition products/impurities."

Correction of a typographical error in the product code:

HOW SUPPLIED section

"9120"

To:

"91201"

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted February 29, 2000).

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 18-298/S-027." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Reproductive and Urologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Jeanine Best, M.S.N., R.N., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

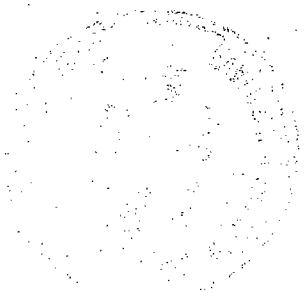
Susan Allen, MD 5/31/00

Susan Allen, M.D., M.P.H.
Acting Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 18-298
HFD-580/Div. Files
HFD-580/J.Best
HFD-580/Rhee/Tran
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-103/ADRA (with labeling)
HFD-40/DDMAC (with labeling)
HFI-20/Press Office (with labeling)
HFD-400/OPDRA (with labeling)
HFD-613/OGD (with labeling)
HFD-21/ACS (with labeling) - ONLY for drug discussed at advisory committee meeting.
HFD-095/DDMS-IMT (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: JAB/May 25, 2000
Initialed by:Rumble,05.25.00/tran,05.25.00/Rhee,05.25.00/Allen,05.29.00
final: JAB?May 30, 2000
filename: N18248S27Apltr.doc

APPROVAL (AP)



CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-248/S-027

FINAL PRINTED LABELING

Oxytocin Injection, USP
Package Insert

Label: Original
NDA 18248 Rec'd 7/12
Reviewed by:

AMERICAN PHARMACEUTICAL PARTNERS, INC.

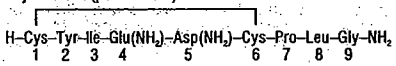
45789B/Revised: January 2000

OXYTOCIN
INJECTION, USP

(SYNTHETIC)

FOR INTRAVENOUS INFUSION OR INTRAMUSCULAR USE

DESCRIPTION:
Each mL of Oxytocin Injection, USP (synthetic), intended for intravenous infusion or intramuscular injection, possesses an oxytocic activity equivalent to 10 USP Oxytocin Units and contains chlorebutanol anhydrous (chloral derivative) 0.5%. This product may contain up to 12.5% decomposition products/impurities. Oxytocin injection (synthetic) is a sterile, clear, colorless solution of oxytocin in Water for Injection prepared by synthesis. Acetic acid may have been added for pH adjustment (pH 3.0-5.0). The structural formula is:



CLINICAL PHARMACOLOGY:
Oxytocin injection (synthetic) acts on the smooth muscle of the uterus to stimulate contractions; response depends on the uterine threshold of excitability. It exerts a selective action on the smooth musculature of the uterus, particularly toward the end of pregnancy, during labor and immediately following delivery. Oxytocin stimulates rhythmic contractions of the uterus, increases the frequency of existing contractions and raises the tone of the uterine musculature. Synthetic oxytocin does not possess the cardiovascular effects, such as elevation of blood pressure, as exhibited by vasopressin found in posterior pituitary injection.

INDICATIONS AND USAGE:

IMPORTANT NOTICE:
Oxytocin Injection, USP (synthetic) is indicated for the medical rather than the elective induction of labor. Available data and information are inadequate to define the benefits to risks considerations in the use of the drug product for elective induction. Elective induction of labor is defined as the initiation of labor for convenience in an individual with a term pregnancy who is free of medical indications.

Antepartum
Oxytocin injection (synthetic) is indicated for the initiation or improvement of uterine contractions, where this is desirable and considered suitable, in order to achieve early vaginal delivery for fetal or maternal

exhibited by vasopressin found in posterior pituitary injection.

INDICATIONS AND USAGE:

IMPORTANT NOTICE:

Oxytocin Injection, USP (synthetic) is indicated for the medical rather than the elective induction of labor. Available data and information are inadequate to define the benefits to risks considerations in the use of the drug product for elective induction. Elective induction of labor is defined as the initiation of labor for convenience in an individual with a term pregnancy who is free of medical indications.

Antepartum

Oxytocin injection (synthetic) is indicated for the initiation or improvement of uterine contractions, where this is desirable and considered suitable, in order to achieve early vaginal delivery for fetal or maternal reasons. It is indicated for (1) induction of labor in patients with a medical indication for the initiation of labor, such as Rh problems, maternal diabetes, pre-eclampsia at or near term, when delivery is in the best interest of mother and fetus or when membranes are prematurely ruptured and delivery is indicated; (2) stimulation or reinforcement of labor, as in selected cases of uterine inertia; (3) adjunctive therapy in the management of incomplete or inevitable abortion. In the first trimester, curettage is generally considered primary therapy. In second trimester abortion, oxytocin infusion will often be successful in emptying the uterus. Other means of therapy, however, may be required in such cases.

Postpartum

Oxytocin injection (synthetic) is indicated to produce uterine contractions during the third stage of labor and to control postpartum bleeding or hemorrhage.

CONTRAINDICATIONS:

Oxytocin injection (synthetic) is contraindicated in any of the following conditions:

- Significant cephalopelvic disproportion;
- Unfavorable fetal positions or presentations which are undeliverable without conversion prior to delivery, i.e., transverse lies;
- In obstetrical emergencies where the benefit-to-risk ratio for either the fetus or the mother favors surgical intervention;
- In cases of fetal distress where delivery is not imminent;
- Prolonged use in uterine inertia or severe toxemia;
- Hypertonic uterine patterns;
- Patients with hypersensitivity to the drug;
- Induction or augmentation of labor in those cases where vaginal delivery is contraindicated, such as cord presentation or prolapse, total placenta previa, and vasa previa.

WARNINGS:

Oxytocin injection (synthetic) when given for induction or stimulation of labor, must be administered only by the intravenous route and with adequate medical supervision in a hospital.

PRECAUTIONS:

General

All patients receiving intravenous oxytocin must be under continuous observation by trained personnel with a thorough knowledge of the drug and qualified to identify complications. A physician qualified to manage any complications should be immediately available.

When properly administered, oxytocin should stimulate uterine contractions similar to those seen in normal labor. Overstimulation of the uterus by improper administration can be hazardous to both mother and fetus. Even with proper administration and adequate supervision, hypertonic contractions can occur in patients whose uteri are hypersensitive to oxytocin.

Except in unusual circumstances, oxytocin should not be administered in the following conditions: prematurity, borderline cephalopelvic disproportion, previous major surgery on the cervix or uterus including Caesarean section, overdistention of the uterus, grand multiparity or invasive cervical carcinoma. Because of the variability of the combinations of factors which may be present in the conditions above, the definition of "unusual circumstances" must be left to the judgement of the physician. The decision can only be made by carefully weighing the potential benefits which oxytocin can provide in a given case against rare but definite potential for the drug to produce hypertonicity or tetanic spasm.

Maternal deaths due to hypertensive episodes, subarachnoid hemorrhage, rupture of the uterus and fetal deaths due to various causes have been reported associated with the use of parenteral oxytocic drugs for induction of labor and for augmentation in the first and second stages of labor.

Oxytocin has been shown to have an intrinsic antidiuretic effect, acting to increase water reabsorption from the glomerular filtrate. Consideration should, therefore, be given to the possibility of water intoxication, particularly when oxytocin is administered continuously by infusion and the patient is receiving fluids by mouth.

Drug Interactions

Severe hypertension has been reported when oxytocin was given three to four hours following prophylactic administration of a vasoconstrictor in conjunction with caudal block anesthesia. Cyclopropane anesthesia may modify oxytocin's cardiovascular effects, so as to produce unexpected results such as hypotension. Maternal sinus bradycardia with abnormal

atrioventricular rhythms has also been noted when oxytocin was used concomitantly with cyclopropane anesthesia.

Carcinogenesis, Mutagenesis, Impairment of Fertility
There are no animal or human studies on the carcinogenicity and mutagenicity of this drug, nor is there any information on its effect on fertility.

Pregnancy Category C.
There are no known indications for use of oxytocin in the first and second trimester of pregnancy other than in relation to spontaneous or induced abortion. Based on the wide experience with this drug and its chemical structure and pharmacological properties, it would not be expected to present a risk of fetal abnormalities when used as indicated.

Nonteratogenic Effects—See **ADVERSE REACTIONS** in the fetus or infant.

Labor and Delivery—See **INDICATIONS AND USAGE.**

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

ADVERSE REACTIONS:
The following adverse reactions have been reported in the mother:
- Anaphylactic reaction
- Postpartum hemorrhage
- Cardiac arrhythmia
- Fatal afibrinogenemia
- Nausea
- Vomiting
- Premature ventricular contractions
- Pelvic hematoma

Excessive dosage or hypersensitivity to the drug may result in uterine hypertonicity, spasm, tetanic contraction or rupture of the uterus.

The possibility of increased blood loss and afibrinogenemia should be kept in mind when administering the drug.

Severe water intoxication with convulsions and coma has occurred, and is associated with a slow oxytocin infusion over a 24-hour period. Maternal death due to oxytocin-induced water intoxication has been reported.

The following adverse reactions have been reported in the fetus or infant:

Due to induced uterine mobility:
- Bradycardia
- Premature ventricular contractions and other arrhythmias
- Permanent CNS or brain damage
- Fetal death

Due to use of oxytocin in the mother:
- Neonatal retinal hemorrhage
- Low Apgar scores at five minutes
- Neonatal jaundice

OVERDOSAGE:
Overdosage with oxytocin injection (synthetic) depends essentially on uterine hyperactivity whether or not due to hypersensitivity to this agent. Hyperstimulation with strong (hypertonic) or prolonged (tetanic) contractions, or a resting tone of 15 to 20 mm H_2O or more between contractions can lead to tumultuous labor, uterine rupture, cervical and vaginal lacerations, postpartum hemorrhage, uteroplacental hypoperfusion and variable deceleration of fetal heart, fetal hypoxia, hypercapnia or death. Water intoxication with convulsions, which is caused by the inherent antidiuretic effect of oxytocin, is a serious complication that may occur if large doses (40 to 50 milliunits/minute) are infused for long periods. Management consists of immediate discontinuation of oxytocin, and symptomatic and supportive therapy.

DOSAGE AND ADMINISTRATION:
Dosage of oxytocin is determined by uterine response. The following dosage information is based upon the various regimens and indications in general use.

Induction or Stimulation of Labor
Intravenous infusion (drip method) is the only acceptable method of administration for the induction or stimulation of labor.

Accurate control of the rate of infusion flow is essential. An infusion pump or other such device and frequent monitoring of strength of contractions and fetal heart rate are necessary for the safe administration of oxytocin for the induction or stimulation of labor. If uterine contractions become too powerful, the infusion can be abruptly stopped, and oxytocic stimulation of the uterine musculature will soon wane.

An intravenous infusion of a non-oxytocin containing solution should be started. Physiologic electrolyte solutions should be used except under unusual circumstances.

To prepare the usual solution for intravenous infusion–one mL (10 units) is combined aseptically with 1,000 mL of a non-hydrating diluent.

The combined solution, rotated in the infusion bottle to insure thorough mixing, contains 10 mU/mL. Add the container with dilute oxytocic solution to the system through the use of a constant infusion pump or other such device to control accurately the rate of infusion.

The initial dose should be no more than 1 to 2 mU/min. The dose may be gradually increased in increments of no more than 1 to 2 mU/min., until a contraction pattern has been established which is similar to normal labor.

The fetal heart rate, resting uterine tone, and the frequency, duration, and force of contractions should be monitored.

The oxytocin infusion should be discontinued immediately in the event of uterine hyperactivity or fetal distress. Oxygen should be administered to the mother.

OVERDOSAGE:
Overdosage with oxytocin injection (synthetic) depends essentially on uterine hyperactivity whether or not due to hypersensitivity to this agent. Hyperstimulation with strong (hypertonic) or prolonged (tetanic) contractions, or a resting tone of 15 to 20 mm H_2O or more between contractions can lead to tumultuous labor, uterine rupture, cervical and vaginal lacerations, postpartum hemorrhage, uteroplacental hypoperfusion and variable deceleration of fetal heart, fetal hypoxia, hypercapnia or death. Water intoxication with convulsions, which is caused by the inherent antidiuretic effect of oxytocin, is a serious complication that may occur if large doses (40 to 50 milliunits/minute) are infused for long periods. Management consists of immediate discontinuation of oxytocin, and symptomatic and supportive therapy.

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The fetal heart rate, resting uterine tone, and the frequency, duration, and force of contractions should be monitored.

The oxytocin infusion should be discontinued immediately in the event of uterine hyperactivity or fetal distress. Oxygen should be administered to the mother. The mother and fetus must be evaluated by the responsible physician.

Control of Postpartum Uterine Bleeding
Intravenous Infusion (Drip Method)—To control postpartum bleeding, 10 to 40 units of oxytocin may be added to 1,000 mL of a nonhydrating diluent and run at a rate necessary to control uterine atony.

Intramuscular Administration—1 mL (10 units) of oxytocin can be given after delivery of the placenta.

Treatment of Incomplete or Inevitable Abortion
Intravenous infusion with physiologic saline solution, 500 mL, or 5% dextrose in physiologic saline solution to which 10 units of oxytocin have been added should be infused at a rate of 20 to 40 drops/minute.

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

HOW SUPPLIED:

Product No.	NDC No.	Oxytocin (synthetic) USP units per mL	Volume
91201*	63323-012-01	10	1 mL in a 3 mL vial
1210	63323-012-10	10	10 mL in a 10 mL vial

*Packaged in a plastic vial.
1 mL size, packaged 25 vials per tray.
Discard unused portion.
10 mL size is a multiple dose vial, packaged 25 vials per tray.
Use only if solution is clear and seal intact.
Store at controlled room temperature 15°-30°C (59°-86°F).
Do not permit to freeze.

AMERICAN PHARMACEUTICAL PARTNERS, INC.
Los Angeles, CA 90024

45789B
Revised: January 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-248/S-027

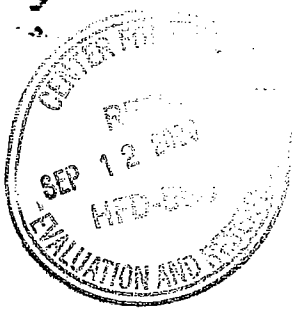
ADMINISTRATIVE DOCUMENTS

AMERICAN PHARMACEUTICAL PARTNERS, INC.

ARCHIVAL

September 6, 2000

ORIGINAL



Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research, HFD-580
Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

S(R-027-FA

NDA NO. REF. NO.
NDA SUPPL FOR

RE: NDA 18-248/S-027
Oxytocin Injection, USP (Synthetic)
10 USP Units/mL
1 mL in 3 mL Plastic Vial (Code 91201)
10 mL in 10-mL Glass Vial (Code 1210)

FPL FOR APPROVED SUPPLEMENT NDA 18-248/S-027

Dear Dr. Rarick:

Reference is made to the supplemental application (S027) dated February 29, 2000, approved May 31, 2000. This supplement provided for an addition of an impurity statement in the **Description** section of the package insert, i.e., **"This product may contain up to 12.5% decomposition products/impurities"**.

As requested in the FDA's communication dated May 31, 2000, American Pharmaceutical Partners, Inc. (APP) is hereby providing 20 copies of the final printed labeling (FPL) which includes the above impurity statement. This labeling was implemented on August 7, 2000.

In compliance with 21 CFR§314.71(b), a true and complete copy of this supplement is being provided simultaneously to the Buffalo District Office.

If you have any questions, please do not hesitate to contact the undersigned at **(708) 547-3615** or Mitchall G. Clark, Vice President of Regulatory Affairs at **(708) 547-3618**.

Sincerely,

Genny Cruz
Senior Regulatory Scientist

REVIEWS COMPLETED
CSO ACTION:
X LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE 5/7/01

2045 NORTH CORNELL AVENUE
MELROSE PARK, IL 60160-1002

MAIN TELEPHONE (708) 343-6100
TELEFAX (708) 547-4429
www.appdrugs.com

Division of Reproductive and Urologic Drug Products

Regulatory Project Manager Review

Application Number: NDA 18-248

Drug Name: Oxytocin Injection, USP

Sponsor: R.W. Johnson Pharmaceutical Research Institute

Material Reviewed (FA):

- Physician Package Insert

Submission Date: September 6, 2000

Receipt Date: September 12, 2000

Background and Summary Description:
The sponsor has submitted final printed labeling (FPL) for their supplemental NDA that was approved on May 31, 2000.

Review:
The FPL submitted is identical to the approved label.

Conclusion:

- The submitted FPL should be Acknowledged and Retained.

_____
Jennifer Mercier
Regulatory Project Manager

Concurrence:

_____
Terri Rumble, B.S.N.
Chief, Project Management Staff

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

/s/

Jennifer L. Mercier
5/21/01 02:54:56 PM
CSO

Terri F. Rumble
5/22/01 11:10:07 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-248/S-027

American Pharmaceuticals Partners, Inc.
Attention: Genny Cruz
Senior Regulatory Scientists
2045 North Cornell Avenue
Melrose Park, IL 60160

Dear Ms. Cruz:

We acknowledge the receipt of your September 6, 2000 submission containing final printed labeling in response to our May 31, 2000 letter approving your supplemental new drug application (NDA) for Oxytocin Injection, USP (Synthetic).

We have reviewed the labeling that you submitted in accordance with our May 31, 2000 letter, and we find it acceptable.

If you have any questions, call Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Susan Allen, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
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/

Daniel A. Shames
5/30/01 01:13:17 PM
For susan Allen

MAY 30 2000

Division of Reproductive and Urologic Drug Products

Regulatory Project Manager Label Review

Application Number: NDA 18-248/S-027

Name of Drug: Oxytocin Injection, USP (Synthetic)

Sponsor: American Pharmaceuticals Partners, Inc.

Material Reviewed:

- Package Insert (draft)

Submission Date: February 29, 2000

Receipt Date: March 8, 2000

Background and Summary Description:
The sponsor submitted a Special Supplement –Changes Being Effected in 30 Days, to provide for a revised package insert, in compliance with 21 CFR § 201.579f)(10), regarding the inclusion of a product impurity statement. Previous labels contained a product impurity statement, but this statement was recently deleted based on evaluation data which showed significantly less amount of impurities than when previously determined using an early analytical method. FDA requested that the label contain a statement based on the actual level of impurities found in the drug product. The sponsor also corrected a typographical error in the product code appearing in the label.

Review:
The sponsor added the following statement to the label:

DESCRIPTION section

"This product may contain up to 12.5% decomposition products/impurities."

The sponsor corrected the product code:

HOW SUPPLIED section

"9102"

To:

"91201"

No other changes in the label were noted.

Conclusions:
Approve draft label as submitted.

Jeanine A. Best, M.S.N., R.N.
Regulatory Project Manager

Concurrence: **Comments:**

5/24/00
Terri Rumble, B.S.N.
Chief, Project Management Staff

5/25/00
Su Tran, Ph.D.
Chemist

5/25/00
Moo-Jhong Rhee, Ph.D.

5/25/00
Susan Allen, M.D., M.P.H.
Acting Director

cc:
Orig. NDA 18-248
HFD-580/Div File
HFD-580/Best
HFD-580/Tran/Rhee
Concurrence:
Drafted: JAB/May 25, 2000/N18248S27labrev.doc
Final:
REGULATORY MANAGER REVIEW

NDA 18-248/S-027

CBE-30 SUPPLEMENT

American Pharmaceuticals Partners, Inc.
Attention: Genny Cruz
Senior Regulatory Scientist
2045 North Cornell Avenue
Melrose Park, IL 60160

MAR 13 2000

Dear Ms. Cruz:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Oxytocin Injection, USP (Synthetic)
NDA Number:	18-248
Supplement Number:	S-027
Date of Supplement:	February 29, 2000
Date of Receipt:	March 8, 2000

This supplemental application, submitted as a "Supplement - Changes Being Effected in 30 days" supplement, proposes to changes to the package insert.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on May 7, 2000 in accordance with 21 CFR 314.101(a).

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

3/14/00

Terri Rumble
Chief, Project Management Staff
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 18-248
HFD-580/Div. Files
HFD-580/J.Mercier
HFD-580/Rhee/Tran

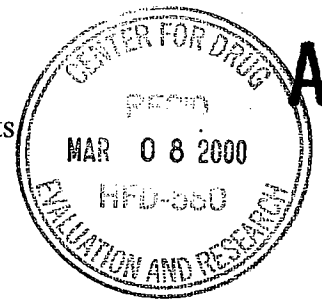
DISTRICT OFFICE

Drafted by: JM/March 10, 2000
Initialed by: Rumble3.13.00/Tran3.13.00/Rhee3.13.00
final: March 14, 2000
filename: 18248S27.WPD

CBE-30 SUPPLEMENT ACKNOWLEDGEMENT (AC)

AMERICAN PHARMACEUTICAL PARTNERS, INC.

February 29, 2000



ARCHIVAL

OK - Reviewed S Tran 3/21/2000

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research, HFD-580
Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

ORIGINAL

RE: NDA 18-248/S-025/S-026
Oxytocin Injection, USP (Synthetic)
10 USP Units/mL
1 mL in 3 mL Plastic vial (Code 91201)
10 mL in 10 mL Glass vial (Code 1210)

AMENDMENT TO SUPPLEMENTS S-025/S-026

NDA NO. 18-248 REF. NO. SLR-027
NDA SUPPL FOR Labelling

Dear Dr. Rarick:

Reference is made to our Special Supplement - Changes Being Effected (S-025) submitted November 12, 1998 under Section 505(b) of the Federal Food Drug and Cosmetic Act and 21 CFR §314.70(c) for the above-mentioned product, approved July 2, 1999. Reference is made to our Labeling Supplement (S-026) submitted December 16, 1998 providing the statement **"This product may contain up to 25% decomposition products/impurities."** in the Description section of the package insert, approved February 22, 1999.

Reference is also made to the amendment for the above supplements (S-025/S-026) submitted February 2, 2000 in which we deleted the above statement in the proposed labeling based on the evaluation of new data which showed significantly less amount of impurities than when previously determined using an early analytical method. Furthermore, reference is made to the telephone conversation between Sue Tran, Chemistry Reviewer (FDA) and Genny Cruz (APP) on February 28, 2000, where the FDA requested that we include the statement **"This product may contain up to 12.5% decomposition products/impurities."**in our proposed labeling based on the actual level of total impurities found in our Oxytocin Injection, USP drug product.

2045 NORTH CORNELL AVENUE
MELROSE PARK, IL 60160-1002

MAIN TELEPHONE (708) 343-6100
TELEFAX (708) 547-4429
www.appdrugs.com

Lisa Rarick, MD, Director
NDA 18-248/S-025/S-026
Oxytocin Injection, USP
February 28, 2000

In this amendment, we are providing in **Attachment 1** a revised copy of the proposed package insert, which includes the statement **"This product may contain up to 12.5% decomposition products/impurities."** in the Description section. The revised insert is the same version as in the February 2, 2000 submission, except, for the change in level of impurities, double-spaced with line entry for ease of review, correction of a typographical error in product code 91201, and the new revision date of February 2000. Provided in **Attachment 2** is an annotated side-by-side comparison of the current and the proposed labeling.

In compliance with 21CFR §314.71(b), we hereby certify that a true and complete field copy of this amendment is provided simultaneously to the Buffalo district office.

Should you have any questions or require additional information concerning this supplement, please do not hesitate to contact the undersigned at **(708) 547-3615** or Nancy Bauer, Associate Director, Regulatory Affairs at **(708) 547-2381**.

Sincerely,

Jenny Cruz

Jenny Cruz
Senior Regulatory Scientist

REVIEWS COMPLETED

CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO

5/31/00

CSO INITIALS DATE

ATTACHMENT B.

9 page(s) of draft labeling has been removed from this portion of the review.