# CENTER FOR DRUG EVALUATION AND RESEARCH

**Application Number** 21-289

## PHARMACOLOGY REVIEW(S)

REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA:

KEY WORDS: ovanex, urofollitropin, FSH
Reviewer Name: Alex Jordan
Division Name: DRUDP
HFD#: 580
Review Completion Date: 3/10/01

Review number: 1
IND/NDA number: NDA 21-289
Serial number/date/type of submission: 00
Information to sponsor: Yes ( ) No (x)
Sponsor (or agent): Ferring Pharm
Manufacturer for drug substance:

Drug: urofollitropin
Code Name:
Generic Name:
Trade Name: Ovanex
Chemical Name:
CAS Registry Number:
Molecular Formula/ Molecular Weight:
Structure:

Relevant INDs/NDAs/DMFs:
Drug Class: gonadotropin
Indication: treatment of infertility
Clinical formulation: each vial contains 75 iu FSH activity — .actose and — Ovanex contains 1-2% LH activity based on bioassay.
Route of administration: sc and im
Proposed clinical protocol or Use: Ovanex is administered for 7 to 12 days to produce ovarian follicular growth in women who do not have primary ovarian failure.

Introduction and drug history: FSH is in a number of approved drug products and has a long history of clinical use. An essentially identical drug, Fertinex, is approved.

Overall Toxicology Summary: Three non-clinical studies were conducted. Report no. 99-2632 was for a single sc inj to female Sprague-Dawley rats (10/gp) at doses of 4, 40 and 400 iu/kg. Animals were examined histologically on day 2 (5 rats) and day 14 (5 rats). Clin chem, hematology and urinalyses were done on days 2 and 14. Only effect was increase in large tertiary follicles.

Report no. 99-3407 was an identical study in female beagle dogs. Only effect was an increase in number and size of ovarian vesicular follicles.

Report 99-6528 was a cardiovascular study in 4 female beagles. Subcutaneous administration of urofollitropin of escalating doses of 4, 40 and 100 iu/kg had no effect on BP, HR, MAP and QA, P-R, QT. R-R, or QTc intervals. Each animal received the vehicle, and all 3 dose levels of test article over 4 separate test days with a 13 day washout period between administrations. Cardiovascular parameters were collected every 30 min for 2 hrs predose, every minute for 1 hr postdose and every 30 min for the remaining 23 hrs of the 24 hr postdose period. Readings were from telemetry devices previously implanted surgically.

OVERALL SUMMARY AND EVALUATION:

Introduction: Urofollitropin is highly purified FSH which is essentially the same drug as Fertinex by Serono and is in approved products such as Pergonal (metropins hMG equal FSH:LH), Metrodin (urofollitropin; purifed hMG to remove LH), Metrodin HP (urofollitropin for injection) and Gonal-F and Follistim (recombinant hFSH alpha and rhFSH beta).
Safety Evaluation: urofollitropin was without effect in the cardiovascular study in dogs. FSH has a long history of human use. There are no safety issues from a toxicological standpoint.

Labeling Review (NDA): Label is satisfactory.

RECOMMENDATIONS: Approval of NDA 21-289

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/s/
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Alexander W. Jordan
6/21/01 08:29:35 AM
PHARMACOLOGIST

APPEARS THIS WAY
ON ORIGINAL

NDA 21-289

A statistical review of Carcinogenicity studies was not conducted.

NDA 21-289

Carcinogenicity studies were waived for this application.