CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-028

SUMMARY REVIEW

Division Director Memo

NDA	22-028
Drug Product	Cosyntropin Injection
Applicant	Sandoz Canada, Inc.
Indication	Diagnostic for screening for adrenal insufficiency

Introduction

This is a 505b2 application for a synthetic adrenocorticotropic hormone (ACTH) comprised of the first 24 N-terminal amino acids of the natural hormone. Endogenous ACTH is secreted from the anterior pituitary hormone and is responsible for the stimulation of production and release of cortisol from the adrenal cortex. ACTH is used therapeutically for a variety of conditions but it is most widely-applied for the diagnosis of adrenal insufficiency where ACTH is administered followed by serial testing of plasma cortisol levels. The applicant submitted this NDA on February 3, 2006 for an indication to be used as a diagnostic agent in the screening for adrenal insufficiency. The application was AE'd on December 26, 2006 due to CMC and microbiology deficiencies. This resubmission provided the data addressing those deficiencies.

Please see the detailed reviews from the CMC, microbiology, clinical pharmacology, clinical, and pharmacology/toxicology reviewers. I am in full concurrence with each discipline and this memo serves as a highlight of data submitted and decisions made.

Clinical

No clinical studies were conducted in this application. However, the applicant conducted a study in healthy volunteers to determine if Cosyntropin is bioequivalent to the reference product, Cortrosyn®. This study has been reviewed by Drs. Wei and Choe in the Office of Clinical Pharmacology and summarized in the clinical reviews by Drs. Lubas and Kehoe. Based on plasma cortisol levels, Cosyntropin was shown to be bioequivalent to Cortrosyn and could be approved on that basis.

Dr. Lubas has made some recommendations to labeling to describe the time points for peak cortisol levels observed in the healthy volunteer population. I agree with inclusion of this information as it may assist clinicians to conduct additional cortisol monitoring in patients in which there is a high index of suspicion for adrenal insufficiency but who have equivocal test results.

Pharmacology/toxicology

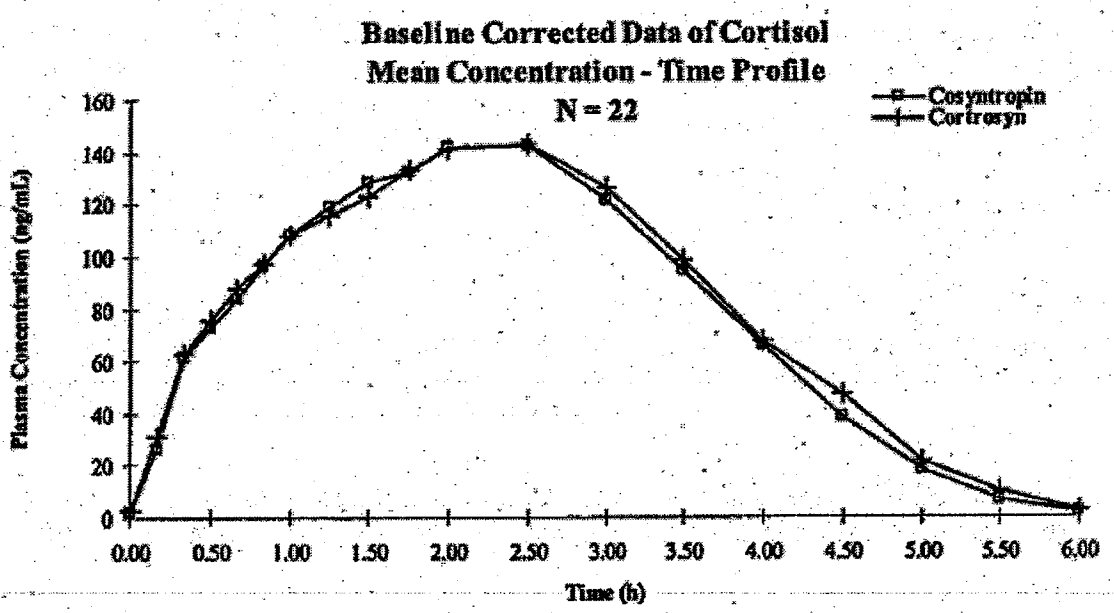
No nonclinical studies were required. The applicant did provide the impurity profile and a non-GLP study in mice. These data were reviewed by Dr. Antonipillai and no concerns precluding approval have been raised.

Clinical Pharmacology

The reference product is Cortrosyn® approved in 1970 under NDA 16-750. The most notable difference between these two products is that the reference product is a lyophilized powder requiring reconstitution prior to administration. Cosyntropin is provided as a sterile aqueous solution. Only a PD assessment for bioequivalence was required between a single 0.25 mg iv dose of Cortrosyn and a single 0.25 mg iv dose

of cosyntropin. Twenty-two healthy volunteers were enrolled in a randomized, single-dose, open-label, cross-over BE study separated by a 5-day washout period. The following graph from Dr. Wei's review shows the Baseline corrected Cortisol results in this BE study.

Figure 1. The time-concentration profiles of Cosyntropin (test drug) and Cortrosyn (LDP) after intravenous administration in healthy human subjects (baseline corrected)



OCP has concluded that bioequivalence was established between the two products based on these findings. They also noted peak cortisol response of 2 to 2.5 hrs and also recommended language describing this response in the label.

CMC and Microbiology
Drs. Haber and Mello have reviewed the materials submitted in response to the AE deficiencies outlined in the December 2006 action letter and have each concluded that this drug product may be approved.

Pediatrics
The reference product label include information for pediatric use and no additional pediatric studies are required for the indication sought.

DMETS and DDMAC
Both DMETS and DDMAC have provided consults and have no objections to the tradename or carton labels.

Regulatory
This 505b2 application has been cleared by the agency's regulatory and legal staff for approval.

Recommendation
Approve.

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/s/

Mary Parks
2/21/2008 06:52:24 PM
MEDICAL OFFICER