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January 30, 2004

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

RE: Citizen's Petition for ANDA Suitability
Ondansetron Hydrochloride Injection

In accordance with 21 CFR 10.20, in the format specified in 21 CFR 10.30, and containing information required by 21 CFR 314.93, the undersigned submits this petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act to obtain permission from the Commissioner of Food and Drugs to submit an abbreviated application for a new drug whose route of administration, dosage form, or strength differ from that of a listed drug.

Action Requested

The petitioner requests that the Commissioner permits an abbreviated new drug application (ANDA) to be filed for Ondansetron Hydrochloride Injection (8 mg/4 mL prefilled syringe).

The listed drugs, Zofran[®] (ondansetron hydrochloride) Injection and Injection Premixed, manufactured by GlaxoSmithKline, are available in three dosage forms:

- (1) 4 mg/2 mL single-dose vial
- (2) 40 mg/20 mL multidose vial
- (3) Premixed, 32 mg/50 mL, in 5% Dextrose (no preservatives) single-dose, flexible plastic container

A copy of the approved labeling for the listed drug Zofran[®] is provided as **Exhibit I**.

The variation requested in this petition is to allow one additional dosage form:

- (1) 8 mg/4 mL prefilled syringe

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The active ingredient (ondansetron hydrochloride) of the proposed drug product is of the same pharmacological or therapeutic class as that of the reference listed drug (Zofran[®]). The proposed drug product can be expected to have the same therapeutic effect as the reference listed drugs when administered to patients for each condition of use in the reference listed drug's labeling for which the applicant seeks approval.

A copy of the proposed labeling for the drug product that is the subject of this petition is provided as **Exhibit II**.

Statement of Grounds

I. Background

Ondansetron HCl injection is a selective 5-HT₃ receptor antagonist. It is indicated for:

- (1) Prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy including high dose cisplatin. Efficacy of the 32 mg single dose beyond 24 hours in these patients has not been established.
- (2) Prevention of postoperative nausea and vomiting.

GlaxoSmithKline markets the injection as a 32 mg/50 mL premix in 5% Dextrose Injection and as a 2 mg/mL concentration in a 2 mL single dose vial and in a 20 mL multi-dose vial.

For the prevention of chemotherapy induced nausea and vomiting, the recommended adult IV dosage is a single 32 mg dose administered 30 minutes before the start of chemotherapy or three 0.15 mg/kg doses (30 minutes before chemotherapy, then 4 and 8 hours after the first ondansetron dose).

For postoperative nausea and vomiting, the recommended adult IV dosage is 4 mg before anesthesia induction or postoperatively¹.

II. Proposed Dosage Forms

Abbott Laboratories plan to file ANDAs for the currently marketed injectable dosage forms. The following additional dosage form is also proposed:

8 mg/4 mL prefilled syringe



III. Medical Rationale for Proposed Forms

Prefilled syringes eliminate the requirement for withdrawing doses from a vial. This minimizes preparation time, which is important when treating a condition that causes patient discomfort such as nausea and vomiting. The syringes are labeled throughout dose preparation and administration. This also reduces the risk of error from drawing an incorrect dose into a syringe. The Luer tip allows for direct intravenous administration through valved ports; a needle may be attached for intramuscular administration or injection through systems that require a needle for intravenous access.

A review of trials by Tramer et al², indicated that an 8 mg dose may be used intravenously for post operative nausea and vomiting. Bernstein and Ong³ determined that 8 mg ondansetron IV combined with dexamethasone was effective in controlling nausea and vomiting in patients receiving moderately and highly emetogenic chemotherapy. Alternative uses include compounding 8 mg admixtures for infusion over 15 minutes for patients weighing approximately 50 kg.

IV. Summary

The proposed 8 mg/4 mL prefilled syringe offers a ready to use system for the clinician in a dose that is used therapeutically.

V. References

1. Prescribing Information. Zofran® (ondansetron hydrochloride) Injection and Injection Premixed. GlaxoSmithKline April 2002 (**Exhibit I**).
2. Tramer MR, Reynolds JM, Moore A, Henry J et al. Efficacy, dose response, and safety of ondansetron in prevention of postoperative nausea and vomiting. *Anesthesiology* 1997; 87:1277-1289 (**Exhibit III**).
3. Bernstein BJ and Ong C. Efficacy of a single 8 mg IV dose of ondansetron hydrochloride for preventing chemotherapy induced emesis. *Am J Health-Syst Pharm* 2002; 59: 650-652 (**Exhibit IV**).

Environmental Impact

We hereby request a categorical exclusion under 21 CFR 25.31(a). The proposed drug product will not be administered at higher dosage levels, for longer duration, or for different indications than that for the listed product. Approval of this petition will not increase the use of the active moiety.

Economic Impact

This information will be submitted if requested by the Commissioner.



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Certification

As required by 21 CFR 10.30(b), certification that this petition is complete and contains all information both favorable and unfavorable, is provided as **Exhibit V**.

We trust that the information presented in this Citizen's Petition is complete and shows our proposed product to be suitable for an abbreviated new drug application.

Sincerely,

ABBOTT LABORATORIES

A handwritten signature in cursive script, appearing to read "JDohnalek".

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