Development of a Bioequivalent Taste Masked Cetirizine HCl 10mg Zydis® Dosage Form using Cyclodextrin

L. Grother, L. Dennis, P. Axe
Catalent Pharma Solutions, Swindon, Wiltshire, SN5 8RU, United Kingdom
Leon.Grother@catalent.com

ABSTRACT SUMMARY
Fast dissolve formulations are a favored dose for certain therapies where patients may require taking medication without ready access to water. Allergy is one such condition: here we describe a novel Orally Disintegrating Tablet (ODT) formulation of cetirizine HCl 10mg developed using cyclodextrin to provide effective taste masking.

Dissolution testing confirmed acceptable release of the cetirizine from the ODT samples. A probe bioequivalence study in 10 healthy subjects demonstrated the bioequivalence to a reference product. The cetirizine 10mg ODT formulation has excellent physical, chemical and microbiological stability when stored at 40°C/75% RH for 6 months. Taste trials conducted by a panel of 30 human volunteers demonstrated that the taste was acceptable.

INTRODUCTION
Cetirizine HCl is a bitter tasting drug indicated for the treatment of allergies. Due to the nature of allergic episodes, medication is often required at unpredictable times and intervals, consequently dose forms such as ODT are frequently preferred by patients due to the greatly enhanced convenience they provide. In order for the drug to be delivered using an ODT such as the Zydis® dosage form, effective taste masking is required. The aim of this study was to investigate if cyclodextrin could be used to taste mask cetirizine HCl 10mg when formulated in a freeze dried ODT (Zydis®). A chemically stable product, bioequivalent to the reference product (Zirtek®) was also a prerequisite for success.

EXPERIMENTAL METHODS
Freeze dried formulations containing various levels and types of cyclodextrin were manufactured using the Zydis® formulation and process.

Dissolution testing was performed on the prototype formulations using USP apparatus II (50rpm) with 900ml purified water. Assay and stability testing was conducted by HPLC. A prediction of taste masking was made by an electronic taste sensing system (Insent® TS-5000Z) fitted with an array of sensors designed to detect various taste stimuli (bitterness, sourness etc). The selected formulation was taken forward to a taste trial using a panel of 30 volunteers. The probe bioequivalence study was a single dose, open label, randomized, two period, two treatment crossover study in 10 healthy adults subjects.

RESULTS AND DISCUSSION
The cyclodextrin was successfully incorporated into the Zydis® dosage form resulting in elegant ODTs with rapid disintegration properties (<2 seconds) compliant with the FDA guidance for industry on Orally Disintegrating Tablets (Dec 2008). Dissolution testing complied with USP criteria with a release profile of cetirizine HCl demonstrating over 85% release in 30 minutes (Figure 1).

Figure 1. Dissolution of Zydis® Cetirizine HCl and Zirtek® comparator.
Taste evaluation using the Insent® 5000Z electronic taste sensing system indicated that taste masking has been achieved. This is demonstrated in Figure 2 by the data points for the Zydis® cetirizine sample formulated with higher levels of cyclodextrin being lower on the x-axis compared to the cetirizine Zydis® data point (control sample without cyclodextrin) than to the pure cetirizine reference.

![Figure 2. Electronic taste sensing system data.](image)

Accelerated stability testing for 6 months at 40°C/75%RH demonstrated acceptable chemical stability, similar to that of the reference product (Table 1). The tablets were white and circular and had a diameter of approximately 15mm and thickness of 4mm. The physical appearance and microbiological purity of the tablets remained the same throughout the stability study.

![Table 1: Stability data of cetirizine HCl products stored for 6 months at 40°C/75% RH](image)

The probe bioequivalence study showed that the Zydis® product was bioequivalent to the Zirtek® comparator (Figure 4).

![Figure 3. Taste trial questionnaire results](image)

![Figure 4. Mean plasma concentrations – Fasted bioequivalence Study (Zydis® vs Zirtek® N=10)](image)

**CONCLUSION**

This study confirms that cyclodextrin can be successfully incorporated into the Zydis® freeze dried ODT to taste mask cetirizine 10mg. A chemically stable product with acceptable dissolution absorption profile. This study has also demonstrated that the Insent® taste sensing system is a useful technique for predicting the taste masking potential of Zydis® formulations. This work confirms the feasibility of developing a commercially viable ODT formulation of cetirizine HCl.

**REFERENCES**