Drug Substance	Budesonide	**SYNOPSIS**	(For national authority use only)
Study Code	D5254C00763		
Date	23 March 2006		

An open single centre study to assess the concentration of budesonide in breast milk from asthmatic women on maintenance treatment with Pulmicort® Turbuhaler® at the dose levels 200 or 400 µg bid

Study centre

This study was conducted at a single center in Sweden.

Study dates

First subject enrolled: 22 September 2004

Last subject completed: 10 October 2005

Phase of Development

Clinical pharmacology (IV)

Objectives

This study was explorative in nature and there was no pre-specified hypothesis. The purpose of the study was to obtain information about the transfer of budesonide from plasma to breast milk and to estimate the exposure of budesonide to the infant by:

- Assessing the concentration of budesonide in breast milk from asthmatic women on maintenance treatment with Pulmicort® Turbuhaler®
- Estimating the exposure of budesonide to the infant from breast milk concentrations
- Calculating pharmacokinetic variables such as AUC, C_{max}, t_{max} and $t_{1/2}$ from breast milk and plasma concentrations, if possible
- Describing milk/plasma budesonide concentration ratio over time
- Evaluating relationships between milk/plasma budesonide concentration ratio and pH, fat and protein content of breast milk
- Measuring plasma concentration of budesonide in infant at one single time point (optional)

Study design

This was an open single-centre study assessing the concentration of budesonide in breast milk and plasma from breast-feeding asthmatic women on maintenance treatment with Pulmicort Turbuhaler. At the clinic, the patients inhaled a single dose of budesonide, 200 µg or 400 µg, according to their normal maintenance treatment. Blood and breast milk samples were collected pre-dose and during 8 hours post dose.

Target subject population and sample size

Asthmatic breast feeding women on maintenance treatment with Pulmicort Turbuhaler 200 or 400 µg bid, aged between 18 and 45 years, having infants aged 1 to 6 months. Eight women were to be included, 4 at each dose level.

Investigational product: dosage, mode of administration and batch numbers

One single oral inhalation of budesonide using Pulmicort Turbuhaler 200 µg (batch EG1335) or Pulmicort Turbuhaler 400 µg (batch EG775 and GG799).

Duration of treatment

Single dose.

Variables

Pharmacokinetics

- Plasma and milk concentrations of budesonide
- Estimated exposure of budesonide to infant based on breast milk concentration data

- Milk/plasma concentration ratio of budesonide
- AUC, C_{max}, t_{max} and $t_{1/2}$ for budesonide in plasma and milk
- Milk pH, fat and protein content of breast milk
- Plasma concentration of budesonide in a single blood sample from the infant (optional)

Safety

- Collection of serious adverse events (SAEs) and discontinuations due to adverse events

Statistical methods

This study was descriptive and did not aim to prove any hypotheses. Descriptive statistics and qualitative analyses were performed at AstraZeneca R&D, Lund.

Subject population

In total 8 asthmatic women and their infants were included in the study, 4 at each dose level (200 µg bid and 400 µg bid) and all subjects completed the study. All women were Caucasians, and their average age was 30.8 (range: 26 to 34) years. Of the infants, 4 were boys and 4 were girls, and their average age was 4.1 (range: 2 to 6) months.

Summary of pharmacokinetic results

- The PK profile of budesonide in lactating women seemed to be similar to the PK profile in non-lactating women (judged by comparison with historical data).
- The PK profile in breast milk followed the plasma profile, supporting passive diffusion as the mechanism of transfer. The mean milk/plasma ratio (based on AUC) was estimated to be 0.46.
- The estimated daily infant doses of budesonide based on average breast milk concentrations were approximately 0.3% of the daily maternal dose for both dose groups. Based on the assumption of complete oral availability of budesonide, the estimated average plasma concentration in the infants was about 600 times lower than the average plasma concentration in the mothers.
- The budesonide breast milk/plasma concentration ratio increased with increasing fat content but was independent of pH and protein content.
- All measured infant plasma concentrations of budesonide were below the LOQ.

Summary of safety results

Only information regarding SAEs and discontinuations due to AEs was collected. There were no SAEs or discontinuations due to AEs.