Teriflunomide has an elimination half-life of 19 days and due to individual variations in drug clearance, it may take up to 2 years to reach plasma concentrations <0.02 μg/mL. For patients taking teriflunomide, the following accelerated elimination procedure (AEP) is recommended for people who are planning a pregnancy, and any case where rapid elimination of teriflunomide is medically desirable:

- Cholestyramine 8 g 3 times daily for 11 days
- Colesevelam HCl, 4 × 625-mg tablets in the morning plus 3 × 625-mg tablets in the evening (7 tablets per day; 4.375 g total daily dose)

At the end of 11 days, plasma concentrations of teriflunomide in plasma were reduced by >98%. A reduction in plasma concentration of >99% is required to reach 0.02 μg/mL of teriflunomide.

The most frequently reported adverse event (AE) occurring during an AEP is gastrointestinal disorder.

**Pharmacokinetics**

- Blood was sampled throughout the study to determine plasma teriflunomide concentrations using a validated liquid chromatography coupled with tandem mass spectrometry method with a lower limit of quantification of 0.01 μg/mL.
- If plasma teriflunomide concentration was <0.02 μg/mL, at Day 17 (end of AEP), subjects received cholestyramine 4 g 3 times daily (12-g total daily dose) as a precautionary measure until teriflunomide concentration was ≤0.02 μg/mL.

**Safety Evaluations**

- Subjects were monitored for AEs, including gastrointestinal events, standard clinical laboratory evaluations (biochemistry, hematology, urinalysis, and coagulation), vital signs (heart rate, systolic and diastolic blood pressure), oral body temperature, 12-lead electrocardiogram (automatic readings), physical examination, and body weight.

**RESULTS**

**Subjects**

A total of 18 subjects were treated and completed the study. Baseline characteristics are summarized in Table 1.

**Pharmacokinetics**

Mean (standard deviation) plasma teriflunomide concentration was 36.3 (4.22) μg/mL at Day 6 (start of AEP) and 1.33 (0.033) μg/mL at Day 17 (end of 11-day AEP), showing a mean decrease of 96.1% (coefficient of variation 3.51%) (Figure 2 and Table 2).

**Safety**

There were no serious or severe AEs, and no AEs led to discontinuation of study treatment.

A summary of AEs related to treatment (or colesevelam HCl) is provided in Table 3.

All subjects recovered from AEs.

**Pharmacokinetics**

- Mean (standard deviation) plasma teriflunomide concentration was 36.3 (4.22) μg/mL at Day 6 (start of AEP) and 1.33 (0.033) μg/mL at Day 17 (end of 11-day AEP), showing a mean decrease of 96.1% (coefficient of variation 3.51%) (Figure 2 and Table 2).

- One subject receiving cholestyramine experienced moderate gastrointestinal disorder AEs.

**CONCLUSIONS**

- Administration of colesevelam HCl for 11 days was sufficient to reduce plasma teriflunomide concentrations by on average >96%.

- Although a direct comparison with cholestyramine has not been conducted, colesevelam HCl may offer an alternative method for accelerated elimination of teriflunomide with improved gastrointestinal tolerability.

**REFERENCES**


**DISCLAIMERS**

Teriflunomide is approved in many countries, including the US and the European Union, for the treatment of moderate to severe relapsing-remitting multiple sclerosis.

This material may contain information that is outside of the approved labeling in some countries.