**Small Reduction in Tedizolid Plasma Exposure in Dialysis End-Stage Renal Disease Patients Is Explained by Variations in Ideal Body Weight**

**Introduction**

- Tedizolid pharmacokinetics in the active moiety tedizolid, is approved in a number of countries, including the United States, Canada, and those of the European Union, for the treatment of acute bacterial skin and skin-structure infections (ABSSSI).
- Population pharmacokinetic (PK) analyses showed that tedizolid PK was similar across a wide range of patient factors, including age, sex, race, body weight, body mass index, and renal or hepatic function.
- Tedizolid phosphate, the prodrug of the active moiety tedizolid, is approved in a number of countries, including the United States.
- Tedizolid exposure was inversely related to the ideal body weight (IBW) among patients with severe renal impairment who were not undergoing dialysis or in the nondialysis, severe renal impairment group (n = 3) and control group (n = 2).

**Methods**

- **Subject selection criteria:**
  - 16-75 years of age
  - Body mass index (BMI) between 18.5 and 40 kg/m²
  - 3 subject groups were studied:
    - Patients with end-stage renal disease (ESRD) requiring long-term hemodialysis
    - A history of stable renal function before dialysis
    - Patients with severe renal impairment who were not undergoing hemodialysis
- **Pharmacokinetic analysis:**
  - Subjects (n = 18) received a single 200 mg intravenous dose of tedizolid phosphate (200 mg IV bolus) in 3 subject groups.
  - Plasma samples were collected from predose through 72 hours postdose.

**Results**

- **Patient baseline renal function:**
  - Mean baseline eGFR was 78.13, 15.9, and 92.6 mL/min/1.73 m² for the dialysis, severe, and control groups, respectively.
- **Distribution of IBW:**
  - The mean IBW was 67.60 kg.
- **Pharmacokinetic parameters:**
  - The mean (SD) IBW was highest among patients in the dialysis group (70.73 [11.52] kg), compared with nondialysis patients with severe renal impairment (65.76 [7.01] kg) and control subjects (61.70 [13.59] kg).
  - The predicted mean (SD) eGFR was 26.90 (9.42), 71.80 (8.40) and 96.40 (17.20) mL/min/1.73 m² for the dialysis, severe, and control groups, respectively.
- **PK parameter most predictive of exposure:**
  - AUC0-∞ = area under the concentration-time curve from time zero to infinity.
  - The mean AUC0-∞ was 10.41 (5.55) µg·h/mL for the dialysis group, compared with 18.50 (7.85) µg·h/mL for patients with severe renal impairment and 36.06 (9.79) µg·h/mL for the control group.
  - The mean AUC0-∞ was calculated using WinNonlin Professional edition, version 5.2 (Certara, Pharsight, Canada).

**Relationship of tedizolid exposure to IBW**

- Tedizolid exposure was inversely related to the IBW (Figure 1).
- Among patients with higher mean IBW, similar PK was seen among the dialysis, severe, and control groups (Figure 2).

**Conclusion**

- This analysis supports the previous conclusion that a tedizolid dose adjustment is not needed for patients with any degree of renal impairment, including those who require hemodialysis.

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**References**

2. Sivextro (tedizolid phosphate) [summary of product characteristics]. Surrey, UK: CIber (UK) Ltd. 2015.

**Clinical Trials**

- NCT01965476 (NCT01965476).