Etrasimod (APD3134) is a once-daily, oral, sphingosine 1-phosphate (SIP) receptor modulator that selectively targets SIP1, SIP2, and SIP3 receptors. SIP receptor modulators reduce lymphocyte egress from lymph nodes, thereby decreasing circulating lymphocytes and subsequent tissue inflammation and damage. Etrasimod is in clinical development for the treatment of immune-mediated inflammatory disorders, such as ulcerative colitis, Crohn’s disease, and atopic dermatitis.

**RESULTS**

- All eight subjects completed the study, and the administered study drug was generally well tolerated.

**Excretion and Mass Balance of Radioactivity in Excreta**

- By 336 hrs post-dose, a mean of 94% of the total administered radioactive dose was recovered in the excreta and found predominantly in the feces (82.0%), with relatively little excreted into urine (4.9%) (Figure 2).

Figure 2. Cumulative excretion of radioactivity in urine and feces.

**Etrasimod oral plasma clearance was low relative to human hepatic blood flow.** PK exposure parameters of etrasimod and total radioactivity showed moderate interindividual variability.

**Metabolite Profile in Excreta**

- The predominant drug-related moieties found in the feces were M3, M6 (oxidation following sulfation), and etrasimod, reflecting 22.1%, 18.9%, and 11.2%, respectively, of the total administered dose; the remainder was spread across multiple other oxidation and glucuronidation (Figure 4).

**CONCLUSIONS**

- The results from this study suggest that etrasimod is both extensively absorbed and metabolized, given the relatively low proportion of intact drug found in the excreta.
- Etrasimod exhibited slow clearance but undergoes extensive metabolization via oxidation, dehydrogenation, sulfation, glucuronidation, and combinations of these reactions.
- Etrasimod is the only single major drug-related entity present in the systemic circulation (i.e., ≤10% of total radioactivity exposure) and is thus expected to be the primary contributor of pharmacologic activity in the clinic.
- Hepato-biliary excretion is the predominant elimination route of etrasimod and its associated metabolites.
- The multiple biotransformation pathways of etrasimod are likely to decrease the risk of PK drug-drug interactions resulting from effects of any coadministered perpetrator drugs.

References


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