TRACLEER® (bosentan)
TRACLEER - Reformulation and Administration of Film-Coated Tablets

SUMMARY

- TRACLEER is available as film-coated tablets and tablets for oral suspension (dispersible tablets).[1]
- Three publications reported on the pharmacokinetics (PK) of bosentan oral suspension.[2-4]
- Data on file and 2 publications assessed the stability of extemporaneously compounded reformulations of TRACLEER film-coated tablets.[5-7]
- The administration of reformulated TRACLEER tablets (orally or via nasogastric tube) has not been formally assessed at this time.
- The decision to reformulate TRACLEER for administration is at the discretion of the treating healthcare provider.
- One randomized trial that reported the administration of a TRACLEER oral solution and 2 case reports that documented the administration of a TRACLEER oral suspension to patients with persistent pulmonary hypertension of the newborn (PPHN) have been included in the REFERENCES section for your review.[8-10]

CLINICAL DATA

PK Studies

Three publications that reported the PK of a bosentan oral suspension were identified.[2-4] In healthy volunteers, a 125 mg oral suspension administered under fasted conditions had similar bioavailability as the 62.5 mg (with or without food) and 125 mg (given as two 62.5 mg tablets with food) tablet formulations.[2] In a study that evaluated the PK and pharmacodynamics of bosentan in healthy human subjects, doses (3 mg-2400 mg) were administered as 100 mL aqueous suspensions. The absolute bioavailability of bosentan was 50% and decreased with doses >600 mg.[3] In another study that assessed the absorption, excretion, and metabolism of bosentan in healthy male subjects, more than 97% of the drug-related material, on average, was recovered within 3.5 days after administering a single oral dose of 500 mg bosentan as 100 mL oral suspension in water.[4]

Stability Studies

Stability of Cut TRACLEER Film-Coated Tablets

Data on file reported the stability of halved tablets. Ten TRACLEER film-coated tablets (62.5 mg) were cut in half and examined in terms of their physical and chemical characteristics. The report found that after 4 weeks of storage, half-cut TRACLEER film-coated tablets met the product specifications and were deemed to be stable.[5]

Stability of Crushed TRACLEER Film-Coated Tablets

Data on file on the stability of crushed TRACLEER film-coated tablets (62.5 mg) found that crushed TRACLEER 62.5 mg tablets were stable for a period of 6 months when stored below 30°C, 65% relative humidity and protected from light. Furthermore, crushed TRACLEER 62.5 mg tablets diluted 1:1 with lactose were stable for a period of 2 months when stored under similar conditions.[5]

Stability of Extemporaneously Compounded Reformulations of TRACLEER Film-Coated Tablets

A study evaluating the stability of a 6.25 mg/mL oral suspension of triturated TRACLEER 62.5 mg film-coated tablets in a 1:1 mixture of FlavorPlus and FlavorSweet compounding vehicles found 94% of the active ingredient was retained when the suspension was stored in

the dark either at room temperature or under refrigeration for 1 month. The suspension was noted to be easily resuspended at various time points by shaking.[6]

A study evaluating the stability of a 6.25 mg/mL oral suspension of crushed TRACLEER 62.5 mg film-coated tablets in water and in *Ora-Blend* diluents found that concentrations dropped to 94% and 92%, respectively, of the starting concentration at day 2 when stored at room temperature. By day 4, the concentrations were approximately 87% when diluted in water and 86% when diluted in *Ora-Blend*. When TRACLEER was compounded with *Ora-Blend* and stored at 4°C, concentration had dropped lower than 89% at day 4.[7]

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 14 January 2025.

REFERENCES

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