PREZISTA® (darunavir)
PREZISTA - Tablet Crushing, Chewing, or Splitting

SUMMARY

- An oral suspension containing PREZISTA 100 mg/mL is commercially available.[1]
- In 2 case reports of patients who received PREZISTA tablets crushed and suspended in water and administered with ritonavir oral solution (1 patient with dysphagia and Candida esophagitis and 1 with a permanent percutaneous endoscopic gastrostomy [PEG-tube]), darunavir (DRV) trough levels were within the therapeutic range, the patients' viral loads (VL) remained suppressed (<40 copies/mL), and their CD4+ counts increased.[2]
- A case report described an intubated 44-year-old male who was administered crushed PREZISTA tablets diluted with 15-20 mL of water via an orogastric tube. After the route of administration was changed from orally-administered tablets to enteral administration of crushed tablets, the patient's VL did not significantly change and the measured DRV trough concentration was within the therapeutic range.[3]

CLINICAL DATA

Case Reports

Scholten et al (2010)[2] presented 2 case reports of patients with swallowing difficulties who received PREZISTA crushed and suspended in water.

Case 1

- A 57-year-old antiretroviral (ARV)-experienced male, who stopped his previous ARVs due to dysphagia from Candida esophagitis and esophageal stenosis, was started on the following regimen:
  - PREZISTA 600 mg twice daily (BID, crushed and suspended in water)
  - Etravirine 200 mg BID (suspended in water)
  - Ritonavir oral solution 100 mg BID
  - Raltegravir 400 mg BID (crushed and suspended in water)
  - Itraconazole oral solution 100 mg BID (which was later switched to fluconazole)
- Baseline VL was 72,551 copies/mL and CD4+ count was 56 cells/mm^3.
- After 1 month of therapy, VL decreased to 102 copies/mL and CD4+ count increased to 111 cells/mm^3.
- Pharmacokinetic parameters were obtained. Trough levels of DRV, etravirine, and ritonavir were measured 10 hours post dose and were within the therapeutic range (Table: Case 1 Drug Levels).

Case 1 Drug Levels[2]

	Drug Levels 10 hours Post Dose (ng/mL)	Average Drug Levels Following Administration (ng/mL)
Darunavir	6950	3539 (median)
Etravirine	336	348 (mean)
Ritonavir	1370	220 (mean)

- The patient remained virologically suppressed (<40 copies/mL) and his CD4+ count increased to 251 cells/mm^3 after 6 months of treatment.

Case 2

- A 48-year-old parapalegic, ARV-experienced female was administered the following regimen via a permanent PEG-tube. This regimen was based on resistance testing after failure on a previous regimen:

    - PREZISTA 600 mg BID (crushed and suspended in water)
    - Ritonavir oral solution 100 mg BID
    - Raltegravir 400 mg BID (crushed and suspended in water)
    - Emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) 300/200 mg once daily (QD, crushed and suspended in water).
- After 28 months of therapy, the patient's VL remained suppressed (<40 copies/mL) and her CD4+ count increased to 528 cells/mm^3 (340-758).
- Pharmacokinetic parameters were obtained. Trough levels of DRV and ritonavir were measured 5 hours post dose at month 24 and 3 hours post dose at month 28. Drug levels were within the therapeutic range at both timepoints (Table: Case 2 Drug Levels).

Case 2 Drug Levels[2]

	Month 24: Drug Levels 5 hours Post Dose (ng/mL)	Month 28: Drug Levels 3 hours Post Dose (ng/mL)
Darunavir	4430	5210
Ritonavir	90	346

Kim et al (2014)[3] described a case report in which crushed PREZISTA tablets were administered to a critically ill patient through an orogastric feeding tube.

- A 44-year-old male with newly-diagnosed (27-days prior) HIV infection, AIDS (baseline VL 269,820 copies/mL; CD4 lymphocytes 9/mm^3), *Pneumocystis jiroveci* pneumonia, cytomegalovirus viremia, and transverse myelitis was admitted to the medical center. The patient developed respiratory distress 1 day after admission and was transferred to the intensive care unit (ICU).
- Fourteen days before admission, the patient started highly-active antiretroviral therapy, consisting of the following agents (administered orally):
    - A fixed-dose combination FTC/TDF 200/300 mg tablet QD
    - PREZISTA 600 mg tablet with ritonavir 100 mg capsule BID
- Additional concomitant oral medications included azithromycin, esomeprazole, and sulfamethoxazole/trimethoprim, and additional concomitant intravenous medications included foscarnet, ganciclovir, and methylprednisolone.
- On ICU day 11, the patient's respiratory status further declined, and endotracheal intubation was required. An orogastric tube was inserted.
- Ritonavir oral solution was substituted for capsules, and the PREZISTA tablet and fixed-dose combination FTC/TDF tablet were crushed to a fine powder.
- The powder was placed into a medicine cup and diluted with 15-20 mL of warm tap water.
- Before administration of the medication, continuous enteral feeding was paused and the orogastric tube was flushed with water.
- The diluted medication was administered with a 60-mL latex-free polypropylene catheter tip syringe for irrigation, followed by another water flush and resumption of enteral nutrition.
- DRV trough concentration was measured after 12 days of orogastric administration of the drug (15.5 hours post dose).
    - The measured trough concentration was 6160 ng/mL (within the therapeutic range).
- VL was measured on ICU day 5 (pre-intubation) and day 18 (post-intubation day 7).
    - No clinically significant change in the VL occurred after the route of PREZISTA administration was altered (79 copies/mL and 125 copies/mL, respectively).
- CD4 lymphocyte counts on ICU day 5 and day 18 were 28 and 3/mm^3, respectively.
- On ICU day 26, acute kidney injury developed. The patient's alanine aminotransferase increased (2.0- to 8.5-fold) throughout the hospital course.
- The patient's clinical condition continued to deteriorate, palliative care was initiated, and the patient died after 27 days of intensive care.

LITERATURE SEARCH

A literature search of Ovid MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File databases (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 13 June 2024.

REFERENCES

1. Data on File. Darunavir. Company Core Data Sheet. Janssen Research & Development, LLC. EDMS-ERI-11052400; December 2021.
2. Scholten S, Mauraschat S, Hindermann S, et al. Administration of darunavir tablets in patients with difficulties swallowing. Poster presented at: the Tenth International Congress on Drug Therapy in HIV Infection; November 7-11, 2010; Glasgow, UK.
3. Kim HC, Muzevich KM, Fulco PP. Orogastric administration of crushed darunavir tablets for a critically ill patient. *Can J Hosp Pharm*. 2014;67(1):39-42.