**PREZISTA® (darunavir)**
**Use of PREZISTA for Postexposure Prophylaxis**

## SUMMARY


- PREZISTA is not indicated for use in postexposure prophylaxis (PEP).[1]
- The United States (US) Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis recommend PREZISTA/ritonavir (r) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) as an alternative regimen for PEP.[2]
- The US Public Health Service Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States recommend PREZISTA/r plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as an alternative regimen for adults and adolescents (13 years or older).[3]
- In a randomized study comparing PREZISTA/r-based PEP with lopinavir (LPV)/r-based PEP in 305 subjects following potential high-risk exposure, there was no difference in early discontinuation rates between groups, although the incidence of grade ≥2 adverse drug reactions was significantly higher in the LPV/r group. No seroconversions were reported.[4]
- Two case reports described use of PREZISTA/r in combination with other antiretroviral treatments (ARTs) for PEP following high-risk occupational exposure to human immunodeficiency virus (HIV)-infected blood.[5,6]
- A case report described the use of ART with TDF, FTC, PREZISTA, and r in a patient diagnosed with HIV.[7]


## US PUBLIC HEALTH SERVICE GUIDELINES

The US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis recommend PREZISTA/r plus 2 NRTIs as an alternative regimen for PEP. The preferred dosing regimen for PREZISTA/r is 800/100 mg once daily (QD).[2]

The US Public Health Service Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States recommend PREZISTA/r plus TDF/FTC as an alternative regimen for adults and adolescents (13 years or older). For adults and adolescents with renal dysfunction (creatinine clearance ≤ 59 ml/min), PREZISTA/r 800/100 mg plus zidovudine/lamivudine (dosages adjusted for renal function) is considered an alternative regimen. For children (3 to 12 years), PREZISTA/r plus TDF/FTC is regarded as an alternative regimen. The dosing for children is based upon the patient's weight and age.[3]

## CLINICAL STUDY

**Fätkenheuer et al (2016)**[4] presented data on the safety and tolerability of PREZISTA/r-based PEP compared to standard-of-care (SOC) PEP in adult subjects following potential high-risk exposure to HIV (N=305).

### Study Design/Methods

- The PEPDar study was an open-label, randomized, multicenter, noninferiority study conducted at 22 sites in Germany.
- Subjects were stratified by risk of exposure (occupational or nonoccupational) and randomized to receive either PREZISTA/r 800/100 mg QD + 2 investigator-selected NRTIs or SOC PEP (2 NRTIs plus either LPV/r or efavirenz, per 2008 German-Austrian guidelines) beginning within 72 hours of exposure for 28-30 days.[4]

- The primary endpoint was early discontinuation (% subjects who discontinued HIV-PEP for >2 consecutive days prior to day 28) for any reason other than documented negative HIV status of the index person.

## Results

- Please refer to Table: Baseline Characteristics (Safety Population)

**Baseline Characteristics (Safety Population)**[4]

| | PREZISTA/r PEP (n=159) | SOC PEP (n=153) |
|---|---|---|
| Male, n (%) | 131 (82) | 125 (82) |
| Median age, years | 33 | 31 |
| Occupational risk, n (%) | 35 (22) | 30 (20) |
| Nonoccupational risk, n (%) | 124 (78) | 123 (80) |
| LPV/r as third agent, n | - | 153 |
| NRTIs used, n | | |
| TDF/FTC | 159 | 146 |
| AZT/3TC | 0 | 6 |
| ABC/3TC | 0 | 1 |
| **Abbreviations:** 3TC, lamivudine; ABC, abacavir; AZT, zidovudine; FTC, emtricitabine; LPV, lopinavir; PEP, postexposure prophylaxis; r, ritonavir; SOC, standard-of-care; TDF, tenofovir disoproxil fumarate. | | |

- Sixty percent of subjects with nonoccupational exposure were exposed through receptive and/or insertive anal sex.
- All subjects randomized to SOC PEP received LPV/r.
- Subjects with occupational exposure began PEP sooner than those with nonoccupational exposure (median [interquartile range]; duration between exposure and start of treatment): 2.2 (0.9-4.2) hours vs 14.0 (5.0-24.0) hours, respectively.
- There was no significant difference in early discontinuation rates by treatment group (PREZISTA/r, 6.5%; SOC PEP, 10.0%).
    - The estimated risk difference for PREZISTA/r PEP-SOC PEP was 3.6% (95% confidence interval [CI]: -14.8 to 7.8; *P*=0.243).

**ADRs (All Grades, ≥5% and of Interest)**[4]

| ADR, n (%) | PREZISTA/r PEP (n=159) | SOC PEP (n=153) |
|---|---|---|
| Any ADR | 108 (68) | 115 (75) |
| Grade 3 ADRs | 4 (3) | 7 (5) |
| GI ADRs | 85 (54) | 105 (69) |
| Abdominal pain | 15 (9) | 11 (7) |
| Diarrhea | 47 (30) | 79 (52) |
| Flatulence | 5 (3) | 11 (7) |
| Nausea | 25 (16) | 42 (28) |
| Vomiting | 12 (8) | 9 (6) |
| Fatigue | 21 (13) | 28 (18) |
| Headache | 19 (12) | 8 (5) |
| Sleep disorder | 0 | 6 (4)[a] |
| Rash | 7 (4) | 4 (3) |
| Rash, generalized | 0 | 1 (1) |
| **Abbreviations**: ADR, adverse drug reaction; GI, gastrointestinal; PEP, postexposure prophylaxis; r, ritonavir; SOC, standard-of-care.<br>[a]*P*=0.013. | | |

- The incidence of sleep disorders (all grades) was significantly higher in the SOC PEP group (n=6) than the PREZISTA/r group (n=0; *P*=0.013). Please refer to Table: ADRs (All Grades, ≥5% and of Interest).
- In addition, the number of subjects with moderate to severe (grade ≥2) adverse drug reactions (ADRs) was significantly higher in the SOC PEP group (n=44) as compared to the PREZISTA/r group (n=25, *P*=0.006).
- No seroconversions were documented in any subject.

## CASE REPORTS

**Siegel et al (2008)**[5] reported a case where PREZISTA was used as part of a PEP regimen administered to a laboratory technologist who received a puncture wound by a capillary tube filled with an HIV-infected patient's blood. The patient's viral genotype/virtual phenotype from 9 months earlier had revealed multiple mutations conferring resistance to all NRTIs, non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) tested. The technologist was started on PREZISTA, r, TDF/FTC, and raltegravir (dosage regimens and duration not provided). The regimen was tolerated without side effects. More than 6 months after exposure, the technologist had no evidence of HIV seroconversion.

**Baraboutis et al (2010)**[6] reported a case of high-grade needlestick exposure of a healthcare worker. A biochemistry technician sustained a deep penetrating needlestick from an automated biochemical analyzer hollow probe where serum from 8 HIV-infected patients and 4 outpatients (HIV status unknown) had just been analyzed. Seven of the 8 HIV-infected patients had an undetectable viral load (VL; <50 copies/mL) at the last measurement, but only 4 of them had VL measurements available from the previous 3 months. The eighth patient had a VL of 59 copies/mL. The healthcare worker was started on PREZISTA, r, TDF/FTC, and raltegravir (dosage regimens not provided). She received the regimen within 3 hours of the exposure and continued for 4 weeks without evidence of clinical or laboratory abnormalities. Testing for HIV was negative at 36 weeks.

**Kohli et al (2024)**[7] reported a case of a 69-year-old male patient with HIV who presented with a 2-year history of pain, swelling, and nail dystrophy in the right middle finger. Initially diagnosed with HIV in 2010, the patient achieved sustained viral suppression on ART with TDF, FTC, PREZISTA, and r. In 2016, he was diagnosed with chronic paronychia affecting the same nail and was treated with a combination of clobetasol propionate, clobetasone butyrate, oxytetracycline, nystatin, and acetic acid soaks. In 2019, a biopsy confirmed Bowen's disease (BD) of the nailbed, with human papillomavirus (HPV)-16 identified by genotyping. In 2021, following progression of the nailbed disease, the affected nailbed was excised, and a skin graft was performed, followed by a repeat excision, with follow-up histology showing no residual BD. The patient received an HPV vaccination (covering HPV-6, -11, -16, and -18). Follow-ups in 2022 revealed no residual lesions or anal intraepithelial neoplasia.

## 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 13 September 2024.

## REFERENCES

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