

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PREZISTA safely and effectively. See Full Prescribing Information for PREZISTA.

PREZISTA (darunavir) Oral Suspension, for Oral use
PREZISTA (darunavir) Tablet, Film Coated for Oral use

Initial U.S. Approval – 2006

-----**RECENT MAJOR CHANGES**-----

- Indications and Usage
 - Pediatric Patients (1.2) 02/2013
- Dosage and Administration
 - Adult Patients (2.1) 11/2012
 - Pediatric Patients (2.2) 02/2013
- Warnings and Precautions
 - Severe Skin Reactions (5.3) 06/2012

-----**INDICATIONS AND USAGE**-----

PREZISTA is a human immunodeficiency virus (HIV-1) protease inhibitor indicated for the treatment of HIV-1 infection in adult patients. PREZISTA is also indicated for the treatment of HIV-1 infection in pediatric patients 3 years of age and older. PREZISTA must be co-administered with ritonavir (PREZISTA/ritonavir) and with other antiretroviral agents. (1)

-----**DOSAGE AND ADMINISTRATION**-----

- Treatment-naïve adult patients and treatment-experienced adult patients with no darunavir resistance associated substitutions: 800 mg (one 800 mg tablet or two 400 mg tablets) taken with ritonavir 100 mg once daily and with food. (2.1)
- Treatment-experienced adult patients with at least one darunavir resistance associated substitution: 600 mg (one 600 mg tablet) taken with ritonavir 100 mg twice daily and with food. (2.1)
- Pediatric patients (3 to less than 18 years of age and weighing at least 10 kg): dosage of PREZISTA and ritonavir is based on body weight and should not exceed the adult dose. PREZISTA should be taken with ritonavir and with food. (2.2)
- PREZISTA/ritonavir is not recommended for use in patients with severe hepatic impairment. (2.3)

-----**DOSAGE FORMS AND STRENGTHS**-----

- 100 mg/mL oral suspension (3)
- 75 mg tablets, 150 mg tablets, 400 mg tablets, 600 mg tablets, and 800 mg tablets (3)

-----**CONTRAINDICATIONS**-----

Co-administration with alfuzosin, dihydroergotamine, ergonovine, ergotamine, methylethylergonovine, cisapride, pimozide, oral midazolam, triazolam, St. John's Wort, lovastatin, simvastatin, rifampin and sildenafil (for treatment of pulmonary arterial hypertension). (4)

- Due to the need for co-administration of PREZISTA with ritonavir, please refer to ritonavir prescribing information for a description of ritonavir contraindications. (4)

-----**WARNINGS AND PRECAUTIONS**-----

- Drug-induced hepatitis (e.g., acute hepatitis, cytolytic hepatitis) has been reported with PREZISTA/ritonavir. Monitor liver function before and during therapy, especially in patients with underlying chronic hepatitis, cirrhosis, or in patients who have pre-treatment elevations of transaminases. Post-marketing cases of liver injury, including some fatalities, have been reported. (5.2, 6)
- Skin reactions ranging from mild to severe, including Stevens-Johnson Syndrome, toxic epidermal necrolysis and acute generalized exanthematous pustulosis, have been reported. Discontinue treatment if severe reaction develops. (5.3, 6)
- Use with caution in patients with a known sulfonamide allergy. (5.4)
- Patients may develop new onset diabetes mellitus or hyperglycemia. Initiation or dose adjustments of insulin or oral hypoglycemic agents may be required. (5.6)
- Patients may develop redistribution/accumulation of body fat (5.7) or immune reconstitution syndrome. (5.8)
- Patients with hemophilia may develop increased bleeding events. (5.9)
- PREZISTA/ritonavir should not be used in pediatric patients below 3 years of age in view of toxicity and mortality observed in juvenile rats dosed with darunavir up to days 23 to 26 of age. (5.11)

-----**ADVERSE REACTIONS**-----

- The most common clinical adverse drug reactions to PREZISTA/ritonavir (incidence greater than or equal to 5% of at least moderate intensity (greater than or equal to Grade 2) were diarrhea, nausea, rash, headache, abdominal pain and vomiting. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Products, LP at 1-800-JANSSEN (1-800-526-7736) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----**DRUG INTERACTIONS**-----

- Co-administration of PREZISTA/ritonavir with other drugs can alter the concentration of other drugs and other drugs may alter the concentrations of darunavir. The potential drug-drug concentrations must be considered prior to and during therapy. (4, 5.5, 7, 12.3).

-----**USE IN SPECIFIC POPULATIONS**-----

- Use during pregnancy only if the potential benefit justifies the potential risk. (8.1)
- Mothers should be instructed not to breastfeed due to the potential for HIV transmission and the potential for serious adverse reactions in nursing infants. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling.

Revised: 02/2013

FULL PRESCRIBING INFORMATION: CONTENTS***FULL PRESCRIBING INFORMATION****1 INDICATIONS AND USAGE**

- 1.1 Adult Patients
- 1.2 Pediatric Patients

2 DOSAGE AND ADMINISTRATION

- 2.1 Adult Patients
- 2.2 Pediatric Patients (age 3 to less than 18 years)
- 2.3 Patients with Hepatic Impairment

3 DOSAGE FORMS AND STRENGTHS

- 3.1 PREZISTA 100 mg/mL Oral Suspension
- 3.2 PREZISTA 75 mg Tablets
- 3.3 PREZISTA 150 mg Tablets
- 3.4 PREZISTA 400 mg Tablets
- 3.5 PREZISTA 600 mg Tablets
- 3.6 PREZISTA 800 mg Tablets

4 CONTRAINDICATIONS**5 WARNINGS AND PRECAUTIONS**

- 5.1 General
- 5.2 Hepatotoxicity
- 5.3 Severe Skin Reactions
- 5.4 Sulfa Allergy
- 5.5 Drug Interactions
- 5.6 Diabetes Mellitus / Hyperglycemia
- 5.7 Fat Redistribution
- 5.8 Immune Reconstitution Syndrome
- 5.9 Hemophilia
- 5.10 Resistance/Cross-Resistance
- 5.11 Pediatric Patients

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience: Treatment-Naïve Adults
- 6.2 Clinical Trials Experience: Treatment-Experienced Adults
- 6.3 Serious ADRs
- 6.4 Patients co-infected with hepatitis B and/or hepatitis C virus
- 6.5 Clinical Trials Experience: Pediatric Patients
- 6.6 Postmarketing Experience

7 DRUG INTERACTIONS

- 7.1 Potential for PREZISTA/ritonavir to Affect Other Drugs

- 7.2 Potential for Other Drugs to Affect Darunavir
- 7.3 Established and Other Potentially Significant Drug Interactions

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Hepatic Impairment
- 8.7 Renal Impairment

10 OVERDOSAGE**11 DESCRIPTION****12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics
- 12.4 Microbiology

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

- 14.1 Description of Adult Clinical Studies
- 14.2 Treatment-Naïve Adult Subjects
- 14.3 Treatment-Experienced Adult Subjects
- 14.4 Pediatric Patients

16 HOW SUPPLIED/STORAGE AND HANDLING**17 PATIENT COUNSELING INFORMATION**

- 17.1 Information About Therapy with PREZISTA
- 17.2 Instructions for Use
- 17.3 Hepatotoxicity
- 17.4 Severe Skin Reactions
- 17.5 Drug Interactions
- 17.6 Fat Redistribution

[*Sections or subsections omitted from the full prescribing information are not listed]

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Adult Patients

PREZISTA[®], co-administered with ritonavir (PREZISTA/ritonavir), and with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection.

This indication is based on analyses of plasma HIV-1 RNA levels and CD4+ cell counts from 2 controlled Phase 3 trials of 48 weeks duration in antiretroviral treatment-naïve and treatment-experienced patients and 2 controlled Phase 2 trials of 96 weeks duration in clinically advanced, treatment-experienced adult patients.

1.2 Pediatric Patients

PREZISTA, co-administered with ritonavir (PREZISTA/ritonavir), and with other antiretroviral agents, is indicated for the treatment of HIV-1 infection in pediatric patients 3 years of age and older [*see Use in Specific Populations (8.4)*].

The indication for treatment-experienced pediatric patients 3 to less than 18 years of age is based on 24-week analyses of plasma HIV-1 RNA levels and CD4+ cell counts from two open-label Phase 2 trials in antiretroviral treatment-experienced pediatric subjects. The indication for treatment-naïve pediatric patients or antiretroviral treatment-experienced patients with no darunavir resistance associated substitutions is based on one open-label Phase 2 trial of 48 weeks duration in antiretroviral treatment-naïve subjects 12 to less than 18 years of age and pharmacokinetic modeling and simulation for patients 3 to less than 12 years of age.

In treatment-experienced adult and pediatric patients, the following points should be considered when initiating therapy with PREZISTA/ritonavir:

- Treatment history and, when available, genotypic or phenotypic testing should guide the use of PREZISTA/ritonavir [*see Clinical Pharmacology (12.4)*].
- The use of other active agents with PREZISTA/ritonavir is associated with a greater likelihood of treatment response [*see Clinical Pharmacology (12.4) and Clinical Studies (14.3)*].

2 DOSAGE AND ADMINISTRATION

2.1 Adult Patients

PREZISTA must be co-administered with ritonavir to exert its therapeutic effect. Failure to correctly co-administer PREZISTA with ritonavir will result in plasma levels of darunavir that will be insufficient to achieve the desired antiviral effect and will alter some drug interactions.

Patients who have difficulty swallowing PREZISTA tablets can use the 100 mg/mL PREZISTA oral suspension.

Treatment-Naïve Adult Patients

The recommended oral dose of PREZISTA is 800 mg (one 800 mg tablet or two 400 mg tablets or 8 mL of the oral suspension) taken with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL of a 80 mg/mL ritonavir oral solution) once daily and with food. An 8 mL darunavir dose should be taken as two 4 mL administrations with the included oral dosing syringe.

Treatment-Experienced Adult Patients

Table 1: Treatment-Experienced Adult Patients

With no darunavir resistance associated substitutions*	With at least one darunavir resistance associated substitution*
Formulations: PREZISTA tablets or oral suspension (100 mg/mL) and ritonavir	

tablets/capsules (100 mg) or solution (80 mg/mL)	
PREZISTA 800 mg (one 800 mg tablet or two 400 mg tablets) or 8 mL [†] (oral suspension) once daily with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL (oral solution) once daily and with food	PREZISTA 600 mg (e.g. one 600 mg tablet) or 6 mL (oral suspension) twice daily with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL (oral solution) twice daily and with food

* V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V and L89V

† An 8 mL darunavir dose should be taken as two 4 mL administrations with the included oral dosing syringe

For antiretroviral treatment-experienced patients genotypic testing is recommended. However, when genotypic testing is not feasible, PREZISTA/ritonavir 600/100 mg twice daily dosing is recommended.

2.2 Pediatric Patients (age 3 to less than 18 years)

Healthcare professionals should pay special attention to accurate dose selection of PREZISTA, transcription of the medication order, dispensing information and dosing instruction to minimize risk for medication errors, overdose, and underdose.

Prescribers should select the appropriate dose of PREZISTA/ritonavir for each individual child based on body weight (kg) and should not exceed the recommended dose for adults.

Before prescribing PREZISTA, children weighing greater than or equal to 15 kg should be assessed for the ability to swallow tablets. If a child is unable to reliably swallow a tablet, the use of PREZISTA oral suspension should be considered.

The recommended dose of PREZISTA/ritonavir for pediatric patients (3 to less than 18 years of age and weighing at least 10 kg is based on body weight (see Tables 2, 3, 4, and 5) and should not exceed the recommended adult dose. PREZISTA should be taken with ritonavir and with food.

The recommendations for the PREZISTA/ritonavir dosage regimens were based on the following:

Twice daily dosing

- Results from two trials in treatment-experienced pediatric subjects 3 to less 18 years of age demonstrating similar darunavir plasma exposures, virologic response rate and safety profile compared to treatment-experienced adults.

Once daily dosing

- Results from one trial in treatment-naïve pediatric subjects 12 to less than 18 years of age demonstrating similar darunavir plasma exposures, virologic response rate and safety profile compared to treatment-naïve adults.
- Results from population pharmacokinetic modeling and simulation in children 3 to less than 12 years of age predicting similar darunavir plasma exposures compared to treatment-naïve adults. Although no clinical trial was conducted to collect exposure-safety data, the predicted exposures from the once daily dosing is supported by exposures observed in a pediatric clinical trial where twice-daily dosing was administered.

Dosing recommendations for treatment-naïve pediatric patients or antiretroviral treatment-experienced pediatric patients with no darunavir resistance associated substitutions

- *Pediatric patients weighing at least 10 kg but less than 15 kg*

The weight-based dose in antiretroviral treatment-naïve pediatric patients or antiretroviral treatment-experienced pediatric patients with no darunavir resistance associated substitutions is PREZISTA 35 mg/kg once daily with ritonavir 7 mg/kg once daily using the following table:

Table 2: Recommended dose for pediatric patients weighing 10 kg to less than 15 kg who are treatment-naïve or treatment-experienced with no darunavir resistance associated substitutions*

Body weight (kg)	Formulation: PREZISTA oral suspension (100 mg/mL) and ritonavir oral solution (80 mg/mL)
	Dose: once daily with food
Greater than or equal to 10 kg to less than 11 kg	PREZISTA 3.6 mL [‡] (350 mg) with ritonavir 0.8 mL (64 mg)
Greater than or equal to 11 kg to less than 12 kg	PREZISTA 4 mL [‡] (385 mg) with ritonavir 0.8 mL (64 mg)
Greater than or equal to 12 kg to less than 13 kg	PREZISTA 4.2 mL (420 mg) with ritonavir 1 mL (80 mg)
Greater than or equal to 13 kg to less than 14 kg	PREZISTA 4.6 mL [‡] (455 mg) with ritonavir 1 mL (80 mg)
Greater than or equal to 14 kg to less than 15 kg	PREZISTA 5 mL [‡] (490 mg) with ritonavir 1.2 mL (96 mg)

* darunavir resistance associated substitutions: V11I, V32I, L33F, I47V, I50V, I54M, I54L, T74P, L76V, I84V and L89V

[‡] The 350 mg, 385 mg, 455 mg and 490 mg darunavir dose for the specified weight groups were rounded up for suspension dosing convenience to 3.6 mL, 4 mL, 4.6 mL and 5 mL, respectively.

Pediatric patients weighing at least 15 kg

Pediatric patients weighing at least 15 kg can be dosed with PREZISTA oral tablet(s) or solution using the following table:

Table 3: Recommended dose for pediatric patients weighing at least 15 kg who are treatment-naïve or treatment-experienced with no darunavir resistance associated substitutions*

Body Weight (kg)	Formulation: PREZISTA tablet(s) and ritonavir capsules or tablets (100 mg)	Formulation: PREZISTA oral suspension (100 mg/mL) and ritonavir oral solution (80 mg/mL)
	Dose: once daily with food	Dose: once daily with food
Greater than or equal to 15 kg to less than 30 kg	PREZISTA 600 mg with ritonavir 100 mg	PREZISTA 6 mL (600 mg) with ritonavir 1.25 mL (100 mg)
Greater than or equal to 30 kg to less than 40 kg	PREZISTA 675 mg with ritonavir 100 mg	PREZISTA 6.8 mL [§] (675 mg) with ritonavir 1.25 mL (100 mg)
Greater than or equal to 40 kg	PREZISTA 800 mg with ritonavir 100 mg	PREZISTA 8 mL [‡] (800 mg) with ritonavir 1.25 mL (100 mg)

* darunavir resistance associated substitutions: V11I, V32I, L33F, I47V, I50V, I54M, I54L, T74P, L76V, I84V and L89V

[§] The 675 mg dose using darunavir tablets for this weight group is rounded up to 6.8 mL for suspension dosing convenience.

[‡] The 6.8 mL and 8 mL darunavir dose should be taken as two (3.4 mL or 4 mL, respectively) administrations with the included oral dosing syringe

Dosing recommendations for treatment-experienced pediatric patients with at least one darunavir resistance associated substitutions

- *Pediatric patients weighing at least 10 kg but less than 15 kg*

The weight-based dose in antiretroviral treatment-experienced pediatric patients with at least one darunavir resistance associated substitution is PREZISTA 20 mg/kg twice daily with ritonavir 3 mg/kg twice daily using the following table:

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.