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) 12/2011
- Dosage and Administration
  - Adult Patients (2.1) 12/2011
  - Pediatric Patients (2.2) 12/2011
- Warnings and Precautions
  - Severe Skin Reactions (5.3) 10/2011
  - Pediatric Patients (5.11) 12/2011

----------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 (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 treatment-experienced adult dose. Do not use once daily dosing in pediatric patients. PREZISTA should be taken with ritonavir twice daily 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, and 600 mg tablets (3)

----------CONTRAINDICATIONS----------

Co-administration with alfuzosin, dihydroergotamine, ergonovine, ergotamine, methylergonovine, 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 and toxic epidermal necrolysis, 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 Tibotec Therapeutics at 1-877-REACH-TT or 1-877-732-2488 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)
  - Pregnancy Registry available. (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: 12/2011

FULL PRESCRIBING INFORMATION: CONTENTS*

[*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)*].

This indication is based on 24-week analyses of plasma HIV-1 RNA levels and CD4+ cell counts from 2 open-label Phase 2 trials in antiretroviral treatment-experienced pediatric patients (one trial in patients 6 to less than 18 years of age and one trial in patients 3 to less than 6 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 (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.

Treatment-Experienced Adult Patients

Treatment-Experienced Adult Patients	
With no darunavir resistance associated substitutions*	With at least one darunavir resistance associated substitution*
PREZISTA 800 mg (two 400 mg tablets or 8 mL†) once daily with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL) once daily and with food	PREZISTA 600 mg (e.g. one 600 mg tablet or 6 mL) twice daily with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL) twice daily and with food

* V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V and L89V
† An 8 mL 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)

Do not use once daily dosing in pediatric patients.

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 treatment-experienced 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 1, 2 and 3) and should not exceed the recommended treatment-experienced adult dose (PREZISTA/ritonavir 600/100 mg twice daily). PREZISTA should be taken with ritonavir twice daily and with food.

Dosing recommendations for pediatric patients weighing at least 10 kg but less than 15 kg

The weight-based dose in pediatric patients weighing less than 15 kg is PREZISTA 20 mg/kg with ritonavir 3 mg/kg which can be dosed using the following table:

Table 1: Recommended Dose for Pediatric Patients with PREZISTA Oral Suspension (100 mg/mL) and Ritonavir Oral Solution* for Pediatric Patients Weighing 10 kg to Less Than 15 kg

Body weight (kg)	Dose (twice daily with food)
Greater than or equal to 10 kg to less than 11 kg	PREZISTA 200 mg (2 mL) with ritonavir 32 mg (0.4 mL)
Greater than or equal to 11 kg to less than 12 kg	PREZISTA 220 mg (2.2 mL) with ritonavir 32 mg (0.4 mL)
Greater than or equal to 12 kg to less than 13 kg	PREZISTA 240 mg (2.4 mL) with ritonavir 40 mg (0.5 mL)
Greater than or equal to 13 kg to less than 14 kg	PREZISTA 260 mg (2.6 mL) with ritonavir 40 mg (0.5 mL)
Greater than or equal to 14 kg to less than 15 kg	PREZISTA 280 mg (2.8 mL) with ritonavir 48 mg (0.6 mL)
*with ritonavir oral solution: 80 mg/mL	

Dosing recommendations for pediatric patients weighing at least 15 kg

Pediatric patients who weigh at least 15 kg and are able to swallow tablets can be dosed using the following table:

Table 2: Recommended Dose for Pediatric Patients with PREZISTA Tablets and Ritonavir Oral Solution or Tablets/Capsules for Pediatric Patients Weighing At Least 15 kg

Body Weight (kg)	Dose (twice daily with food)
Greater than or equal to 15 kg to less than 30 kg	PREZISTA 375 mg with ritonavir* 50 mg (0.6 mL)
Greater than or equal to 30 kg to less than 40 kg	PREZISTA 450 mg with ritonavir* 60 mg (0.75 mL)
Greater than or equal to 40 kg	PREZISTA 600 mg with ritonavir† 100 mg
*with ritonavir oral solution: 80 mg/mL † with ritonavir capsules or tablets: 100 mg	

Pediatric patients who weigh at least 15 kg but are unable to swallow tablets can be dosed using the following table:

Table 3: Recommended Dose for Pediatric Patients with PREZISTA Oral Suspension (100 mg/mL) and Ritonavir Oral Solution* for Pediatric Patients Weighing At Least 15 kg

Body Weight (kg)	Dose (twice daily with food)
Greater than or equal to 15 kg to less than 30 kg	PREZISTA 375 mg† (3.8 mL) with ritonavir 50 mg (0.6 mL)
Greater than or equal to 30 kg to less than 40 kg	PREZISTA 450 mg# (4.6 mL) with ritonavir 60 mg (0.75 mL)
Greater than or equal to 40 kg	PREZISTA 600 mg (6 mL) with ritonavir 100 mg (1.25 mL)
*with ritonavir oral solution: 80 mg/mL † The 375 mg dose refers to the dose using darunavir tablets for this weight group, which is rounded off to 3.8 mL for suspension dosing. # The 450 mg dose refers to the dose using darunavir tablets for this weight group, which is rounded off to 4.6 mL for suspension dosing.	

Do not use PREZISTA/ritonavir in pediatric patients below 3 years of age [*see Warnings and Precautions (5.11) and Nonclinical Toxicology (13.2)*].

2.3 Patients with Hepatic Impairment

No dose adjustment is required in patients with mild or moderate hepatic impairment. No data are available regarding the use of PREZISTA/ritonavir when co-administered to subjects with severe hepatic impairment; therefore, PREZISTA/ritonavir is not recommended for use in patients with severe hepatic impairment [*see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)*].

3 DOSAGE FORMS AND STRENGTHS

3.1 PREZISTA 100 mg/mL Oral Suspension

PREZISTA (darunavir) 100 mg/mL oral suspension is supplied as a white to off-white opaque suspension for oral use, containing darunavir ethanolate equivalent to 100 mg of darunavir per mL of suspension.

3.2 PREZISTA 75 mg Tablets

PREZISTA (darunavir) 75 mg tablets are supplied as white, caplet-shaped, film-coated tablets containing darunavir ethanolate equivalent to 75 mg of darunavir per tablet. Each tablet is debossed with “75” on one side and “TMC” on the other side.

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