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
PREZISTA (darunavir) tablet, for oral use
Initial U.S. Approval: 2006

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

Dosage and Administration (2.1, 2.2, 2.4, 2.5)	06/2016
Contraindications (4)	09/2016
Warnings and Precautions, Resistance/Cross-Resistance (5.10)	Removed 06/2016

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

PREZISTA is a human immunodeficiency virus (HIV-1) protease inhibitor indicated for the treatment of HIV-1 infection in adult and 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----------

- Testing:
  - In treatment-experienced patients, treatment history genotypic and/or phenotypic testing is recommended prior to initiation of therapy with PREZISTA/ritonavir to assess drug susceptibility of the HIV-1 virus (2.1, 12.4)
  - Monitor serum liver chemistry tests before and during therapy with PREZISTA/ritonavir. (2.1, 2.2, 5.2)
- Treatment-naïve adult patients and treatment-experienced adult patients with no darunavir resistance associated substitutions: 800 mg (one 800 mg tablet) taken with ritonavir 100 mg once daily and with food. (2.3)
- 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. (2.3)
- Pregnant patients: 600 mg (one 600 mg tablet) taken with ritonavir 100 mg twice daily and with food. (2.4)
- 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. (2.5)
- PREZISTA/ritonavir is not recommended for use in patients with severe hepatic impairment. (2.6)

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

- Oral suspension: 100 mg per mL (3)
- Tablets: 75 mg, 150 mg, 600 mg, and 800 mg (3)

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

- Co-administration of PREZISTA/ritonavir is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events (narrow therapeutic index). (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)
- Skin reactions ranging from mild to severe, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms and acute generalized exanthematous pustulosis, have been reported. Discontinue treatment if severe reaction develops. (5.3)
- 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 or immune reconstitution syndrome. (5.7, 5.8)
- Patients with hemophilia may develop increased bleeding events. (5.9)
- PREZISTA/ritonavir is not recommended 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. (5.10)

----------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 concentrations of other drugs and other drugs may alter the concentrations of darunavir. The potential drug-drug interactions must be considered prior to and during therapy. (4, 5.5, 7, 12.3)

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

- Pregnancy: Total darunavir exposures were generally lower during pregnancy compared to postpartum period. The reduction in darunavir exposures during pregnancy were greater for once daily dosing compared to the twice daily dosing regimen. (8.1, 12.3)
- Lactation: Women infected with HIV should be instructed not to breastfeed due to the potential for HIV transmission. (8.2)
- Pediatrics: Not recommended for patients less than 3 years of age. (8.4)

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

Revised: 09/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PREZISTA®, co-administered with ritonavir (PREZISTA/ritonavir), in combination with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection in adult and pediatric patients 3 years of age and older *[see Use in Specific Populations (8.4) and Clinical Studies (14)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Testing Prior to Initiation of PREZISTA/ritonavir

In treatment-experienced patients, treatment history, genotypic and/or phenotypic testing is recommended to assess drug susceptibility of the HIV-1 virus *[see Microbiology (12.4)]*. Refer to *Dosage and Administration (2.3), (2.4) and (2.5)* for dosing recommendations.

Appropriate laboratory testing such as serum liver biochemistries should be conducted prior to initiating therapy with PREZISTA/ritonavir *[see Warnings and Precautions (5.2)]*.

2.2 Monitoring During Treatment with PREZISTA/ritonavir

Patients with underlying chronic hepatitis, cirrhosis, or in patients who have pre-treatment elevations of transaminases should be monitored for elevation in serum liver biochemistries, especially during the first several months of PREZISTA/ritonavir treatment *[see Warnings and Precautions (5.2)]*.

2.3 Recommended Dosage in 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 per mL PREZISTA oral suspension.

Treatment-Naïve Adult Patients

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

Treatment-Experienced Adult Patients

The recommended oral dosage for treatment-experienced adult patients is summarized in Table 1.

Baseline genotypic testing is recommended for dose selection. However, when genotypic testing is not feasible, PREZISTA 600 mg taken with ritonavir 100 mg twice daily is recommended.

Table 1: Recommended PREZISTA/ritonavir Dosage in Treatment-Experienced Adult Patients

Baseline Resistance	Formulation and Recommended Dosing	
	PREZISTA tablets with ritonavir tablets or capsule	**PREZISTA oral suspension (100 mg/mL) with ritonavir oral solution (80 mg/mL)**
With no darunavir resistance associated substitutions*	One 800 mg PREZISTA tablet with one 100 mg ritonavir tablet/capsule, taken once daily with food	8 mL† PREZISTA oral suspension with 1.25 mL ritonavir oral solution, taken once daily with food
With at least one darunavir resistance associated substitutions*, or with no baseline resistance information	One 600 mg PREZISTA tablet with one 100 mg ritonavir tablet/capsule, taken twice daily with food	6 mL PREZISTA oral suspension with 1.25 mL ritonavir oral solution, taken twice daily 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

2.4 Recommended Dosage During Pregnancy

The recommended dosage in pregnant patients is PREZISTA 600 mg taken with ritonavir 100 mg twice daily with food.

PREZISTA 800 mg taken with ritonavir 100 mg once daily should only be considered in certain pregnant patients who are already on a stable PREZISTA 800 mg with ritonavir 100 mg once daily regimen prior to pregnancy, are virologically suppressed (HIV-1 RNA less than 50 copies per mL), and in whom a change to twice daily PREZISTA 600 mg with ritonavir 100 mg may compromise tolerability or compliance.

2.5 Recommended Dosage in 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 pediatric clinical trial data and population pharmacokinetic modeling and simulation *[see Use in Specific Populations (8.4) and Clinical Pharmacology (12.3)]*.

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 suspension 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) Dose: once daily with food	Formulation: PREZISTA oral suspension (100 mg/mL) and ritonavir oral solution (80 mg/mL) 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

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