HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NORVIR safely and effectively. See full prescribing information for NORVIR.

NORVIR (ritonavir) capsules, soft gelatin for oral use
Initial U.S. Approval: 1996

WARNING: DRUG-DRUG INTERACTIONS LEADING TO POTENTIALLY SERIOUS AND/OR LIFE THREATENING REACTIONS
See full prescribing information for complete boxed warning

Co-administration of NORVIR with several classes of drugs including sedative hypnotics, antiarrhythmics, or ergot alkaloid preparations may result in potentially serious and/or life-threatening adverse events due to possible effects of NORVIR on the hepatic metabolism of certain drugs. Review medications taken by patients prior to prescribing NORVIR or when prescribing other medications to patients already taking NORVIR [see Contraindications (4), Warnings and Precautions (5.1), Drug Interactions (7), and Clinical Pharmacology (12.3)].

RECENT MAJOR CHANGES

Contraindications (4)	11/2016
Warnings and Precautions	
Diabetes Mellitus/Hyperglycemia (5.7)	11/2016

INDICATIONS AND USAGE

NORVIR is an HIV protease inhibitor indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. (1)

DOSAGE AND ADMINISTRATION

- Dose modification for NORVIR is necessary when used with other protease inhibitors. (2)
- Adult patients: 600 mg twice-daily with meals if possible. (2.1)
- Pediatrics patients: The recommended twice daily dose for children greater than one month of age is based on body surface area and should not exceed 600 mg twice daily with meals if possible. (2.2)

DOSAGE FORMS AND STRENGTHS

- Capsule, Soft Gelatin: 100 mg. (3)

CONTRAINDICATIONS

- NORVIR is contraindicated in patients with known hypersensitivity to ritonavir (e.g., toxic epidermal necrolysis, Stevens-Johnson syndrome) or any of its ingredients. (4)
- Co-administration with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations may be associated with serious and/or life-threatening events. (4)
- Co-administration with drugs that significantly reduce ritonavir. (4)

WARNINGS AND PRECAUTIONS

The following have been observed in patients receiving NORVIR:

- The concomitant use of NORVIR and certain other drugs may result in known or potentially significant drug interactions. Consult the full prescribing information prior to and during treatment for potential drug interactions. (5.1, 7.2)
- Hepatic Reactions: Fatalities have occurred. Monitor liver function before and during therapy, especially in patients with underlying hepatic disease, including hepatitis B and hepatitis C, or marked transaminase elevations. (5.2, 8.6)
- Pancreatitis: Fatalities have occurred; suspend therapy as clinically appropriate. (5.3)
- Allergic Reactions/Hypersensitivity: Allergic reactions have been reported and include anaphylaxis, toxic epidermal necrolysis, Stevens-Johnson syndrome, bronchospasm and angioedema. Discontinue treatment if severe reactions develop. (5.4, 6.2)
- PR interval prolongation may occur in some patients. Cases of second and third degree heart block have been reported. Use with caution with patients with preexisting conduction system disease, ischemic heart disease, cardiomyopathy, underlying structural heart disease or when administering with other drugs that may prolong the PR interval. (5.5, 12.3)
- Total cholesterol and triglycerides elevations: Monitor prior to therapy and periodically thereafter. (5.6)
- Patients may develop new onset or exacerbations of diabetes mellitus, hyperglycemia. (5.7)
- Patients may develop immune reconstitution syndrome. (5.8)
- Patients may develop redistribution/accumulation of body fat. (5.9)
- Hemophilia: Spontaneous bleeding may occur, and additional factor VIII may be required. (5.10)

ADVERSE REACTIONS

The most frequently reported adverse drug reactions among patients receiving NORVIR alone or in combination with other antiretroviral drugs were gastrointestinal (including diarrhea, nausea, vomiting, abdominal pain (upper and lower), neurological disturbances (including paresthesia and oral paresthesia), rash, and fatigue/asthenia (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AbbVie Inc. at 1-800-633-9110 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Co-administration of NORVIR can alter the concentrations of other drugs. The potential for drug-drug interactions must be considered prior to and during therapy. (4, 5.1, 7, 12.3)

USE IN SPECIFIC POPULATIONS

- Lactation: Women infected with HIV should be instructed not to breastfeed due to the potential for HIV transmission (8.2).

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

Revised: 12/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: DRUG-DRUG INTERACTIONS LEADING TO POTENTIALLY SERIOUS AND/OR LIFE THREATENING REACTIONS

Co-administration of NORVIR with several classes of drugs including sedative hypnotics, antiarrhythmics, or ergot alkaloid preparations may result in potentially serious and/or life-threatening adverse events due to possible effects of NORVIR on the hepatic metabolism of certain drugs. Review medications taken by patients prior to prescribing NORVIR or when prescribing other medications to patients already taking NORVIR *[see Contraindications (4), Warnings and Precautions (5.1), Drug Interactions (7),* and *Clinical Pharmacology (12.3)]*.

1 INDICATIONS AND USAGE

NORVIR is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

2 DOSAGE AND ADMINISTRATION

NORVIR is administered orally in combination with other antiretroviral agents. It is recommended that NORVIR be taken with meals if possible.

General Dosing Guidelines

Patients should be aware that frequently observed adverse events, such as mild to moderate gastrointestinal disturbances and paraesthesias, may diminish as therapy is continued.

Dose modification for NORVIR

Dose reduction of NORVIR is necessary when used with other protease inhibitors: atazanavir, darunavir, fosamprenavir, saquinavir, and tipranavir.

Prescribers should consult the full prescribing information and clinical study information of these protease inhibitors if they are co-administered with a reduced dose of ritonavir *[see Warnings and Precautions (5.1),* and *Drug Interactions (7)]*.

2.1 Adult Patients

Recommended Dosage for treatment of HIV-1

The recommended dosage of ritonavir is 600 mg twice daily by mouth. Use of a dose titration schedule may help to reduce treatment-emergent adverse events while maintaining appropriate ritonavir plasma levels. Ritonavir should be started at no less than 300 mg twice daily and increased at 2 to 3 day intervals by 100 mg twice daily. The maximum dose of 600 mg twice daily should not be exceeded upon completion of the titration.

2.2 Pediatric Patients

The recommended dosage of ritonavir in children greater than 1 month is 350 to 400 mg per m^2 twice daily by mouth and should not exceed 600 mg twice daily. Ritonavir should be started at 250 mg per m^2 twice daily and increased at 2 to 3 day intervals by 50 mg per m^2 twice daily. If patients do not tolerate 400 mg per m^2 twice daily due to adverse events, the highest tolerated dose may be used for maintenance therapy in combination with other antiretroviral agents, however, alternative therapy should be considered. The use of NORVIR oral solution is recommended for children greater than 1 month who cannot swallow capsules. Please refer to the NORVIR oral solution full prescribing information for pediatric dosage and administration.

3 DOSAGE FORMS AND STRENGTHS

- NORVIR (ritonavir) capsules, soft gelatin

White soft gelatin capsules imprinted with the “a” logo, 100 and the code DS, providing 100 mg of ritonavir.

4 CONTRAINDICATIONS

- When co-administering NORVIR with other protease inhibitors, see the full prescribing information for that protease inhibitor including contraindication information.
- NORVIR is contraindicated in patients with known hypersensitivity (e.g., toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome) to ritonavir or any of its ingredients.
- NORVIR 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 reactions.
- NORVIR is contraindicated with drugs that are potent CYP3A inducers where significantly reduced lopinavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance and cross-resistance.

Table 1. Drugs that are Contraindicated with NORVIR

Drug Class	Drugs Within Class That Are Contraindicated With NORVIR**	Clinical Comments
$Alpha_1$-adrenoreceptor antagonist	Alfuzosin HCL	Potential for hypotension.
Antiarrhythmics	Amiodarone, dronedarone, flecainide, propafenone, quinidine	Potential for cardiac arrhythmias.
Antifungal	Voriconazole	Voriconazole is contraindicated with ritonavir doses of 400 mg every 12 hours or greater due to the potential for loss of antifungal response.

Anti-gout	Colchicine[a]	Potential for serious and/or life-threatening reactions in patients with renal and/or hepatic impairment.
Antipsychotics	Lurasidone Pimozide	Potential for serious and/or life - threatening reactions.Potential for serious and/or life-threatening reactions such as cardiac arrhythmias.
Ergot Derivatives	Dihydroergotamine, ergotamine, methylergonovine	Potential for acute ergot toxicity characterized by vasospasm and ischemia of the extremities and other tissues including the central nervous system.
GI Motility Agent	Cisapride	Potential for cardiac arrhythmias.
Herbal Products	St. John's Wort (hypericum perforatum)	May lead to loss of virologic response and possible resistance to NORVIR or to the class of protease inhibitors.
HMG-CoA Reductase Inhibitors	Lovastatin, simvastatin	Potential for myopathy including rhabdomyolysis.
PDE5 inhibitor	Sildenafil[b] (Revatio®) only when used for the treatment of pulmonary arterial hypertension (PAH)	Potential for sildenafil-associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope.
Sedative/hypnotics	Oral midazolam[c], triazolam	Prolonged or increased sedation or respiratory depression.

[a] see Drug Interactions (7), *Table 4* for colchicine doses in patients with normal hepatic and renal function.
[b] see Drug Interactions (7), *Table 4* for co-administration of sildenafil in patients with erectile dysfunction.
[c] see Drug Interactions (7), *Table 4* for parenterally administered midazolam.

DOCKET ALARM

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.