



独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

**Elvitegravir/cobicistat/emtricitabine/tenofovir
alafenamide fumarate**

**Darunavir ethanolate/cobicistat
Darunavir**

**ethanolate/cobicistat/emtricitabine/tenofovir
alafenamide fumarate**

Doravirine

**Dolutegravir sodium/rilpivirine
hydrochloride**

**Bictegravir sodium/emtricitabine/tenofovir
alafenamide fumarate**

Rilpivirine

Rilpivirine hydrochloride

Rilpivirine

**hydrochloride/emtricitabine/tenofovir
alafenamide fumarate**

Apalutamide

Enzalutamide

March 17, 2026

Non-proprietary name

See attachment

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
Contact: <https://www.pmda.go.jp/english/contact/0001.html>



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Brand name (marketing authorization holder)

See attachment

Japanese market launch

See attachment

Indications

See attachment

Summary of revisions

a. to c., e. to i.

1. "Patients receiving the following drugs: Apalutamide and enzalutamide" should be added to 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)
2. "Apalutamide" and "Enzalutamide" should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

d.

1. "Patients receiving the following drugs: Apalutamide" should be added to 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)
2. "Apalutamide" should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

j.

1. Patients receiving the drugs listed in a. to i. should be added to 2. CONTRAINDICATIONS. (This drug is contraindicated to the following patients.)
2. The drugs listed in a. to i. should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

k.

1. Patients receiving the drugs listed in a. to c. and e. to i. should be added to 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)
2. The drugs listed in a. to c. and e. to i. should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

Investigation results and background of the revision

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Pharmacokinetic effects of the co-administration of anti-HIV drugs listed in a. to i. and apalutamide or enzalutamide * were evaluated. Co-administration with apalutamide or enzalutamide may lead to a decrease in the blood concentration of elvitegravir, cobicistat, darunavir, doravirine, bicitgravir, and rilpivirine, causing loss of antiviral activity as well as the development of resistance. As a result of consultation with expert advisors, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Of note, opinions regarding the impacts of contraindicating co-administration of anti-HIV drugs listed in a. to i. and apalutamide and enzalutamide in clinical settings were sought from relevant academic societies, confirming no specific major problems.

*: The pharmacokinetic effects of co-administration of doravirine and enzalutamide were not evaluated because co-administration of these drugs is already contraindicated.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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Attachment

Number	Non-proprietary name	Brand name	Marketing authorization holder	Date of Initial Marketing in Japan	Indications
a.	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate	Genvoya Combination Tablets	Gilead Sciences K.K.	July 2016	HIV-1 infection
b.	Darunavir ethanolate/cobicistat	Prezcobix Combination Tablets	Janssen Pharmaceutical K.K.	January 2017	HIV infection
c.	Darunavir ethanolate/cobicistat/emtricitabine/tenofovir alafenamide fumarate	Symtuza Combination Tablets	Janssen Pharmaceutical K.K.	July 2019	HIV-1 infection
d.	Doravirine	Pifeltro Tablets 100 mg	MSD K.K.	February 2020	HIV-1 infection
e.	Dolutegravir sodium/rilpivirine hydrochloride	Juluca Combination Tablets	Viiv Healthcare K.K.	December 2018	HIV-1 infection
f.	Bictegravir sodium/emtricitabine/tenofovir alafenamide fumarate	Biktarvy Combination Tablets	Gilead Sciences K.K.	April 2019	HIV-1 infection

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g.	Rilpivirine	Rekambys Aqueous Suspension for IM Injection 600 mg, 900 mg	Janssen Pharmaceutical K.K.	June 2022	HIV-1 infection
h.	Rilpivirine hydrochloride	Edurant Tablets 25 mg	Janssen Pharmaceutical K.K.	June 2012	HIV-1 infection
i.	Rilpivirine hydrochloride/ emtricitabine/tenofovir alafenamide fumarate	Odefsey Combination Tablets	Janssen Pharmaceutical K.K.	September 2018	HIV-1 infection
j.	Apalutamide	Erleada Tablets 60 mg	Janssen Pharmaceutical K.K.	May 2019	○ Castration-resistant prostate cancer without remote metastasis ○ Metastatic prostate cancer
k.	Enzalutamide	Xtandi Tablets 40 mg, 80 mg	Astellas Pharma Inc.	May 2014 (market launch of Xtandi Capsules 40 mg)	○ Castration-resistant prostate cancer ○ Metastatic prostate cancer