

Summary of Investigation Results

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate, Darunavir ethanolate/cobicistat, Darunavir ethanolate/cobicistat/emtricitabine/tenofovir alafenamide fumarate, Doravirine, Doravirine/islatravir hydrate, Dolutegravir sodium/rilpivirine hydrochloride, Bictegravir sodium/emtricitabine/tenofovir alafenamide fumarate, Rilpivirine, Rilpivirine hydrochloride, Rilpivirine hydrochloride/emtricitabine/tenofovir alafenamide fumarate, Lenacapavir sodium, Ivosidenib, Encorafenib, and Mitotane

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	See Attachment.	See Attachment.
Japanese market launch	See Attachment.	
Indications	See Attachment.	
Summary of revisions	a. to c., f. to j. 1. "Patients receiving the following drugs: Ivosidenib, encorafenib, and mitotane" should be added to 2. CONTRAINDICATIONS (This drug is contraindicated in the following patients.) 2. "Ivosidenib," "Encorafenib," and "Mitotane" should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS. d., e., k., l. 1. "Patients receiving the following drugs: Ivosidenib and encorafenib" should be added to 2. CONTRAINDICATIONS (This drug is contraindicated in the following patients.) 2. "Ivosidenib" and "Encorafenib" should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS. m., n. 1. Patients receiving the drugs listed in a. to l. should be added to 2. CONTRAINDICATIONS (This drug is contraindicated in the following patients.) 2. 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS should be newly established to add the drugs listed in a. to l. o.	

	1. Patients receiving the drugs listed in a. to c. and f. to j. should be added to 2. CONTRAINDICATIONS (This drug is contraindicated in the following patients.) 2. Drugs listed in a. to c. and f. to j. should be added to 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.
Investigation results and background of the revision	Pharmacokinetic effects of the co-administration of anti-HIV drugs listed in a. to l. and ivosidenib, encorafenib, or mitotane * were evaluated. Co-administration with ivosidenib, encorafenib, or mitotane may lead to a decrease in the blood concentration of elvitegravir, cobicistat, darunavir, doravirine, bictegravir, rilpivirine, and lenacapavir, causing a reduction 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 l. and ivosidenib, encorafenib, or mitotane in clinical settings were sought from relevant academic societies, confirming no specific major problems.

*: The pharmacokinetic effects of co-administration of doravirine, doravirine/islatravir hydrate, or lenacapavir sodium with mitotane 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).

Attachment

No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	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.	Doravirine/islatravir hydrate	Idvynso Combination Tablets	MSD K.K.	April 2026	HIV-1 infection
f.	Dolutegravir sodium/rilpivirine hydrochloride	Juluca Combination Tablets	Viiiv Healthcare K.K.	December 2018	HIV-1 infection
g.	Bictegravir sodium/emtricitabine /tenofovir alafenamide fumarate	Biktarvy Combination Tablets	Gilead Sciences K.K.	April 2019	HIV-1 infection
h.	Rilpivirine	Rekambyl Aqueous Suspension for IM Injection 600 mg, 900 mg	Janssen Pharmaceutical K.K.	June 2022	HIV-1 infection
i.	Rilpivirine hydrochloride	Edurant Tablets 25 mg	Janssen Pharmaceutical K.K.	June 2012	HIV-1 infection
j.	Rilpivirine hydrochloride/ emtricitabine/tenofovir alafenamide fumarate	Odefsey Combination Tablets	Janssen Pharmaceutical K.K.	September 2018	HIV-1 infection
k.	Lenacapavir sodium	Sunlenca Tablets 300 mg	Gilead Sciences K.K.	September 2023	Multidrug-resistant HIV-1 infection
l.	Lenacapavir sodium	Sunlenca Subcutaneous Injection 463.5 mg	Gilead Sciences K.K.	September 2023	Multidrug-resistant HIV-1 infection

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.

m.	Ivosidenib	Tibsovo Tablets 250 mg	Nihon Servier Co., Ltd.	June 2025	○ <i>IDH1</i> mutation-positive acute myeloid leukemia ○ <i>IDH1</i> mutation-positive unresectable biliary tract cancer that has progressed after cancer chemotherapy
n.	Encorafenib	Braftovi Capsules 50 mg, 75 mg	Ono Pharmaceutical Co., Ltd.	Braftovi Capsules 50 mg: February 2019 Braftovi Capsules 75 mg: November 2020	○ Unresectable melanoma with <i>BRAF</i> gene mutation ○ Unresectable, advanced or recurrent <i>BRAF</i> mutation-positive colorectal cancer ○ Unresectable <i>BRAF</i> mutation-positive thyroid cancer that has progressed after cancer chemotherapy ○ Unresectable <i>BRAF</i> mutation-positive anaplastic thyroid cancer
o.	Mitotane	Opeprim	Yakult Honsha Co., Ltd.	March 1984	○ Adrenal gland cancer ○ Cushing's syndrome for which surgery is not indicated