



GILEAD

For People Taking BIKTARVY[®] Combination Tablets

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Introduction

This leaflet was created for people who take BIKTARVY Combination Tablets. It includes information about the characteristics of BIKTARVY Combination Tablets, how to take BIKTARVY Combination Tablets, what to do if you forget to take BIKTARVY Combination Tablets, the side effects of BIKTARVY Combination Tablets, and precautions for taking BIKTARVY Combination Tablets. Read this leaflet carefully before taking BIKTARVY Combination Tablets.

The treatment of HIV (human immunodeficiency virus) infection is aimed at inhibiting the multiplication of HIV, thereby preventing the onset of AIDS. BIKTARVY Combination Tablets is one of the drugs called “anti-HIV medicines” that suppress the multiplication of HIV.

To safely achieve the adequate efficacy of an anti-HIV medicine, it is important to take it correctly.

A medical decision needs to be made based on your own particular circumstances before starting the administration of BIKTARVY Combination Tablets.

Listen carefully to the explanation provided by your healthcare provider (doctor, nurse, or pharmacist) and follow their instructions.

If you have any questions about the administration of BIKTARVY Combination Tablets, consult your healthcare provider (doctor, nurse, or pharmacist).

For People Taking BIKTARVY Combination Tablets

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What are BIKTARVY Combination Tablets?

BIKTARVY is a medicine for HIV infection that suppresses the multiplication of the virus in the blood¹⁾.

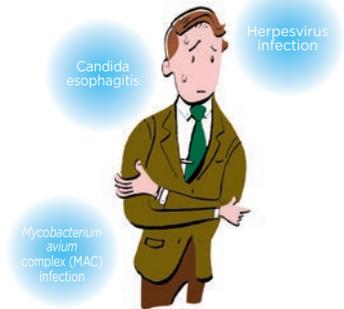
When BIKTARVY Combination Tablets are administered and the multiplication of HIV in the blood is suppressed, immune-compromised patients recover some of their immune function and are less likely to acquire opportunistic infections²⁾.

Note 1) Amount of virus in the blood

The amount of virus in the blood is represented by the viral count in 1 mL of plasma. It indicates the treatment start time and/or the effects of the anti-HIV medicines. The goal of treatment is to maintain a viral concentration that is below the detection limit over a long period of time.

Note 2) Opportunistic infections

Signifies infections caused by weakly pathogenic microorganisms that do not cause infections in people with normal immune function. Opportunistic infections include candida esophagitis, herpesvirus infection, and *Mycobacterium avium* complex (MAC) infection.



How to take BIKTARVY Combination Tablets

- Take one tablet of BIKTARVY once a day, with or without food.
- To avoid forgetting to take BIKTARVY, and to ensure that it is taken at a regular interval, consult your doctor and decide the time of administration.
→ p.10 "How to prevent missing a dose"

Tablet of BIKTARVY and how to store BIKTARVY Combination Tablets

BIKTARVY is a purple-brown tablet, as shown in the pictures on the right (actual size).

[Blister packs]

- Keep out of the reach of children.
- Keep tablets in the packs until use.
- A desiccant is placed below each tablet.
Never accidentally swallow a desiccant.



[Bottles]

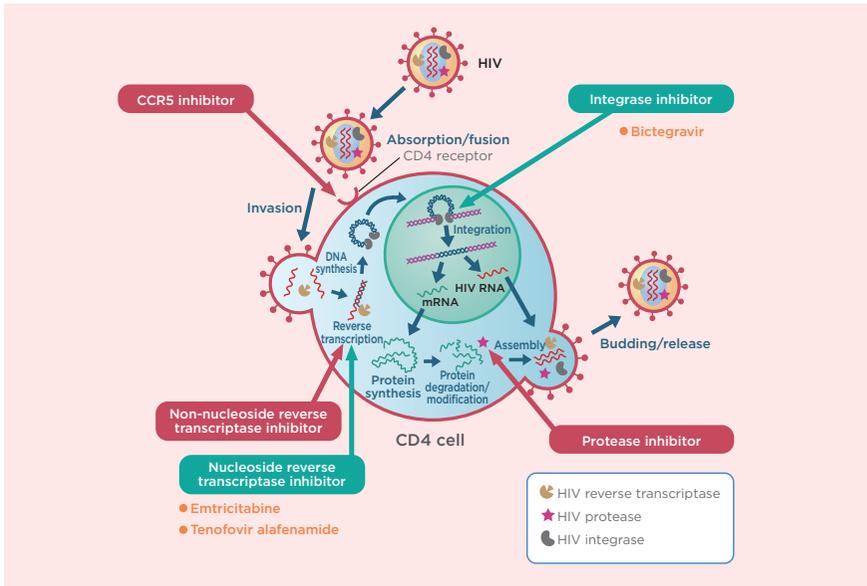
- Keep out of the reach of children.
- Keep tablets in the prescribed container.
- Do not remove the desiccant from the container.
- Store at room temperature, away from moisture.
- To open the container

- 1) While pressing down on the cap,
- 2) Turn it counterclockwise.



Effects of BIKTARVY Combination Tablets

BIKTARVY Combination Tablets contain three active ingredients: bictegrovir, emtricitabine, and tenofovir alafenamide. These active ingredients block the mechanisms involved in the multiplication of HIV, thereby suppressing the multiplication of the virus. There is more than one viral multiplication mechanism, and it is more effective to block two or more mechanisms at the same time. This is why it is popular to administer two or more active ingredients at the same time.



For better treatment going forward

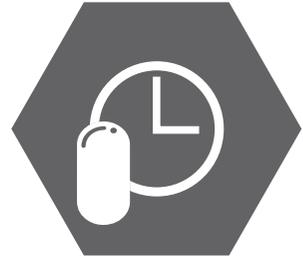
To achieve adequate effects, it has become popular to use more than one anti-HIV medicine in combination. The combination of medicines that best suits the patient is selected to achieve convenience of administration, taking into account the number of tablets to be taken, the number of daily doses, the influence of meals, the size of the medicine, and other factors.

Some medicines may not be administered concomitantly with other medicines.³⁾ In such cases, anti-HIV medicines are selected after confirming the conditions and ongoing therapies of the patient.

Note 3) The influence of the concomitant administration of medicines is called "interaction."



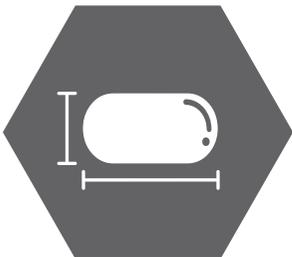
The number of tablets



The number of daily doses



The influence of meals



The size of the tablet



Interaction

BIKTARVY Combination Tablets is a drug that combines three anti-HIV medicines in one tablet.

Take one tablet of BIKTARVY once a day.

BIKTARVY Combination Tablets can be taken at the determined time of administration, whether or not you have eaten a meal.

For example, you may decide to take it before breakfast, if you eat breakfast at the same time every day. Alternatively, you may decide to take it before leaving home for work, if you leave home at the same time every day. Determine the time of administration based on your work habits or lifestyle.

→ p.10 “How to prevent missing a dose”

BIKTARVY tablets have a major axis of approx. 15 mm and a minor axis of approx. 8 mm.

A BIKTARVY tablet is of the exact size as shown in the pictures below.



→ p.3 “What are BIKTARVY Combination Tablets?”

To suppress the multiplication of HIV, it is important to continue taking the medicine. To help patients continue taking BIKTARVY Combination Tablets, they have characteristics as described above.

Be sure to take one tablet of BIKTARVY once a day, at the determined time, without forgetting.

For the interaction of BIKTARVY Combination Tablets, see the next page (p.7).

If you are taking other medicines

If you are taking medicines or supplements that are listed below, their concomitant use with BIKTARVY Combination Tablets may cause side effects, or may decrease the efficacy of BIKTARVY Combination Tablets. If you are taking any medicines, supplements, or health foods, or if you plan to use new medicines, supplements, or health foods, inform and consult with your healthcare provider (doctor or pharmacist) to take necessary measures.

Medicines and foods that should not be taken concomitantly with BIKTARVY Combination Tablets

 **Do not take BIKTARVY Combination Tablets if you are taking the following medicines or foods.**

Antimycobacterials	Rifampicin (Rifadin®)
Anticonvulsants	Carbamazepine (Tegretol®, etc.), phenobarbital (Phenobar®, etc.), phenytoin (Aleviatin®, etc.), fosphenytoin (Fostoin®)
Herbal products	St. John's wort

BIKTARVY Combination Tablets cannot be used concomitantly with other anti-HIV medicines. In particular, do not take BIKTARVY Combination Tablets if you are taking anti-HIV medicines, etc. that contain the following ingredients.

- Other medicines that contain **emtricitabine** (Truvada® Combination Tablets, Emtriva® Capsules, Complera® Combination Tablets, Stribild® Combination Tablets)
- Other medicines that contain **tenofovir disoproxil fumarate (TDF)** (Truvada® Combination Tablets, Viread® Tablets, Complera® Combination Tablets, Stribild® Combination Tablets, Tenozet® Tablets)
- Other medicines that contain **tenofovir alafenamide fumarate (TAF)** (Descovy® Combination Tablets, Vemlidy® Tablets, Odefsey® Combination Tablets)
- Other medicines that contain **lamivudine** (Epzicom® Combination Tablets, Combivir® Combination Tablets, Epivir® Tablets, Triumeq® Combination Tablets, Zefix® Tablets)

Medicines and foods that require consultation with your doctor/pharmacist before concomitant use

 **If you are taking the following medicines or foods, consult your healthcare provider (doctor/pharmacist) in advance.**

Antiarrhythmics	Pilsicainide (Sunrythm®, etc.)
Antimycobacterials	Rifabutin (Mycobutin®)
Anti-HIV medicines	Atazanavir (Reyataz®)
Hypoglycemic agents	Metformin (Metgluco®, etc.)
Antivirals	Aciclovir (Zovirax®, etc.), valaciclovir hydrochloride (Valtrex®, etc.), valganciclovir hydrochloride (Valixa®)
Antacids that contain magnesium or aluminum; preparations that contain iron or calcium (contained in supplements, calcium preparations, iron preparations, antacids, laxatives, sucralfates, etc.)	

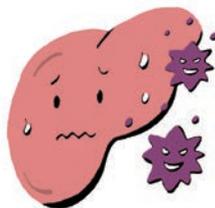
Precautions for taking BIKTARVY Combination Tablets

If you are infected with hepatitis B

- If you are infected with the hepatitis B virus (HBV)⁴⁾ and take BIKTARVY Combination Tablets, your hepatitis may relapse or rapidly deteriorate when you stop taking BIKTARVY Combination Tablets. Therefore, before starting the administration of BIKTARVY Combination Tablets, you need to confirm that you are not infected with HBV.

Note 4) Hepatitis B virus (HBV)

The hepatitis B virus (HBV) causes chronic hepatitis B. HBV multiplies continuously in hepatocytes. Therefore, it must be noted that even healthy people can be carriers of HBV. It is estimated that 1.5 million Japanese people are infected with HBV.



The following people cannot take BIKTARVY Combination Tablets.

- People who used to take bicitgravir, emtricitabine, and/or tenofovir alafenamide, which are the active ingredients of BIKTARVY Combination Tablets, and discontinued their use due to hypersensitivity
- People who are taking rifampicin, carbamazepine, phenobarbital, phenytoin, fosphenytoin, and/or herbal products that contain St. John's wort
→ p.7 "If you are taking other medicines"

Precautions are required for people with a remarkable degree of impaired kidney function.

- If your creatinine clearance is < 30 mL/minute, consult your doctor.

Precautions are required for people with a remarkable degree of impaired liver function.

If you plan to become pregnant, consult your doctor.

- The effects of the administration of BIKTARVY Combination Tablets during pregnancy on a pregnant woman or the fetus are unknown. If you plan to become pregnant, be sure to consult your doctor.
- Avoid breastfeeding while you are taking BIKTARVY Combination Tablets.



What should you do if you miss a dose of BIKTARVY Combination Tablets?

The most important thing is to take measures to prevent missing a dose.

Not missing a dose is important for continuously suppressing the multiplication of HIV. Missing a dose not only compromises the effects of BIKTARVY Combination Tablets, but may also result in the virus acquiring resistance (i.e., it may become impossible to suppress the multiplication of the virus with the medicine).



Should you miss a dose of BIKTARVY Combination Tablets...

If you miss a dose, take one dose of BIKTARVY Combination Tablets (one tablet) as soon as possible after you realize that you have forgotten to take the medicine. Subsequently, continue taking BIKTARVY Combination Tablets as scheduled.

If it is close to the time for the next administration when you realize that you have missed a dose, wait until the next administration and take one dose as scheduled.

Never take two doses (two tablets) at a time.

Even if you have missed a dose, never take two doses (two tablets) at a time. If you do take two or more tablets at a time and feel any abnormal effects, immediately consult your healthcare provider (doctor or pharmacist).



How to prevent missing a dose

To prevent missing a dose, it is key to determine the time of administration.

Consult your doctor and determine the time of administration to prevent missing a dose, and be sure to take the medicine at that time. For example, if you get up at the same time every day, decide to take the medicine as soon as you get up, so that you can minimize the risk of missing a dose.

Measures to prevent missing a dose

- Use the alarm function on your smartphone, etc.
- Keep an administration record on your smartphone or pocketbook

It is also important to confirm in advance what to do if you forget to take BIKTARVY Combination Tablets.

→ p.9 “What should you do if you miss a dose of BIKTARVY Combination Tablets?”



Use an alarm function



Use a pocketbook



Gilead Sciences, Inc. operates an official LINE account that provides reminder and other drug adherence support tools:

Side effects of BIKTARVY Combination Tablets

If you feel any physical abnormality including the following side effects while you are taking BIKTARVY Combination Tablets, consult your doctor immediately.

Typical side effects

Headache, nausea, diarrhea, and other typical side effects may occur.

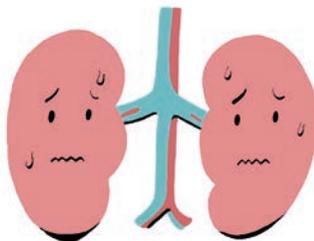


Serious side effects

Kidney failure or severe kidney dysfunction

The administration of BIKTARVY Combination Tablets may result in kidney failure or severe kidney dysfunction. The following conditions may occur due to kidney failure or severe kidney dysfunction.

- Decreased urine
- Swelling
- Weariness
- Decreased muscular strength
- Bone pain
- Increased urine
- Thirst
- Excessive thirst



Regular kidney function tests will be performed, and you may be required to discontinue the administration of BIKTARVY Combination Tablets if abnormality is observed. If any of the following applies, inform your doctor in advance.

- History of kidney disease
- Ongoing administration of a medicine that imposes a burden on the kidneys

Lactic acidosis

If any of the following conditions occur due to the administration of BIKTARVY Combination Tablets, discontinue the administration and immediately consult your doctor regarding the possibility of lactic acidosis.

- Headache
- Drowsiness
- Lowering of consciousness

Hepatomegaly (fatty liver)

Severe hepatomegaly (fatty liver) may be caused by serious lactic acidosis. If any of the following conditions are observed, suggesting suspected lactic acidosis or liver dysfunction, contact your doctor.

- Flap-like trembling of hands
- Nausea
- Pain or tenderness in the upper right abdomen
- Yellowing of skin

Changes in your immune system

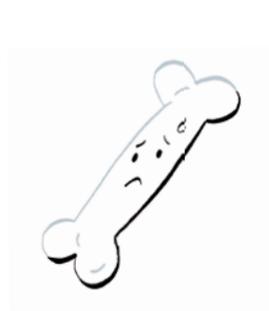
After you start taking BIKTARVY Combination Tablets, an inflammatory reaction (fever, diarrhea) may be caused in response to opportunistic infection, etc., due to the recovery of your immunity. Autoimmune diseases may also be caused.

Decreased bone density

Your bone density may decrease due to the administration of BIKTARVY Combination Tablets.

Skin discoloration

Your skin may become discolored, mainly on the palms, due to the administration of BIKTARVY Combination Tablets.



Attaining U=U status

Learn about U=U and undergo continuous treatment for attaining U=U status

- “Undetectable equals Untransmittable” (U=U) is a status where the amount of HIV in the blood (“viral load”) is maintained at an undetectable level through treatment, which signifies that the virus is untransmittable through sex.¹⁻⁴
- To attain U=U status, it is critical to undergo continuous treatment and not skip any hospital visits.

1 Rodger A, et al.: JAMA 2016; 316(2): 171.

2 Rodger AJ, et al.: Lancet 2019; 393: 2428.

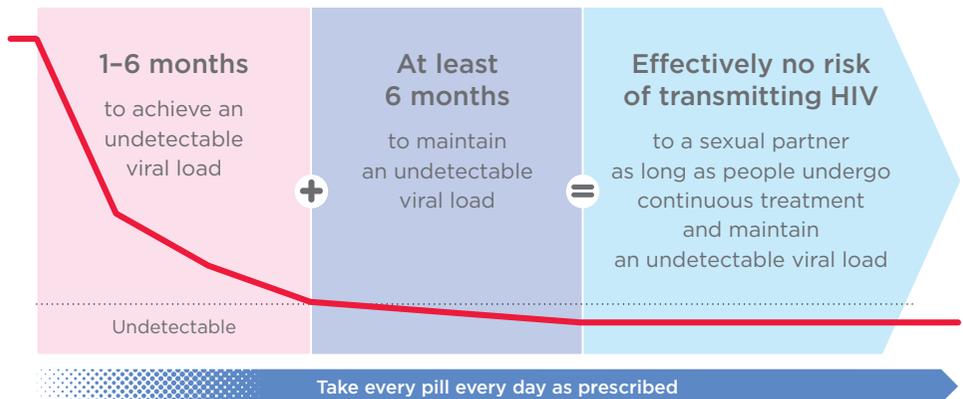
3 Bavinton BR, et al.: Lancet HIV 2018; 5(8): e438.

4 HIV Treatment Guidelines. March 2022.

People who maintain an undetectable viral load for six months or longer through treatment with anti-HIV drugs cannot transmit HIV through sex.

It takes about six months before an undetectable viral load is attained, depending on the types of drugs used. To continuously and reliably suppress HIV, the appropriate drugs must be taken as prescribed.

Reference: <https://www.preventionaccess.org/consensus>, accessed on June 1, 2023



Adapted from U=U Japan Project, “What is U=U?”

<https://hiv-uujapan.org/summary/>, accessed on June 1, 2023.

Masazumi Yamaguchi: JaNP + News Letter 2019, No. 40,

https://www.janpplus.jp/uploads/NL_vol40_web.pdf, accessed on June 1, 2023.

Note that people may transmit HIV through sex if drug adherence is compromised or if treatment is interrupted. Also, remember that infection with other sexually transmitted diseases is still possible even if an undetectable HIV load is maintained, and take the following additional precautions.

Precautions in daily life

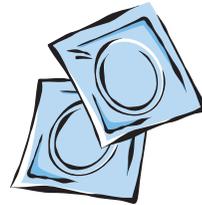
Protecting others

- Do not donate your blood.
- Consult your doctor concerning pregnancy and childbirth.
- Avoid the shared use of toothbrushes and razors to make sure that your bodily fluids do not come into contact with another person's mucous membranes or wounds. Use condoms when you have sexual intercourse.



Protecting yourself

- U=U only applies to HIV. You can still be infected with hepatitis B, chlamydia, gonorrhea, syphilis, and other sexually transmitted diseases. Be sure to use condoms properly when you have sexual intercourse, as infection with any of the above can have unfavorable effects on your immune system and the progression of your disease.



Are there any other precautions?

Take the following precautions.

- Be sure to continue your periodic hospital visits while you are being treated with drugs. Do not stop taking your drugs or change how you take them except on the advice of your doctor.
- Do not provide your drugs to others.

Information sources concerning HIV infection

Information concerning HIV infection is available on the following websites.

- AIDS Clinical Center, National Center for Global Health and Medicine
<https://www.acc.ncgm.go.jp/> (Japanese version only)
- AIDS Medical Center, National Hospital Organization
Osaka National Hospital
<https://osaka.hosp.go.jp/department/khac/>
(Japanese version only)
- AIDS Prevention Information Network
<https://api-net.jfap.or.jp/> (Japanese version only)
- Gilead Sciences “To Patients and Their Families”
<https://www.hiv-pt-portal.jp> (Japanese version only)



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