Odefsey

FACT SHEET

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Summary

Odefsey is the name of a fixed-dose co-formulation of three anti-HIV drugs: tenofovir alafenamide (TAF), emtricitabine (FTC) and rilpivirine. Odefsey can be used by itself as combination therapy for people with HIV who have not taken anti-HIV drugs in the past and who have HIV that is not resistant to any of the drugs in Odefsey. General side effects of Odefsey include headache and sleep problems. Odefsey is taken once daily with a meal.

What is Odefsey?

Odefsey is the name of a pill that contains the following three anti-HIV drugs:

- Rilpivirine (Edurant), which belongs to a class of drugs called non-nukes or NNRTIs
- TAF (tenofovir alafenamide), which belongs to a class of drugs called nucleotide analogues
- FTC (emtricitabine, Emtriva), which belongs to a class of drugs called nucleoside analogues, or nukes

Because Odefsey contains these three medications, it can be used as a once-daily treatment for HIV infection in some HIV-positive people (see How do people with HIV use Odefsey?).

How does Odefsey work?

When HIV infects a cell, it takes control of that cell. HIV then forces the cell to make many more copies of the virus. To make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced the production of HIV slows.

All three medicines in Odefsey interfere with an enzyme called reverse transcriptase, which is used by HIV-infected cells to make more HIV. Since Odefsey inhibits, or reduces, the activity of this enzyme, this drug causes HIV-infected cells to greatly slow down producing new viruses.

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How do people with HIV use Odefsey?

Because it contains three anti-HIV drugs, Odefsey is considered antiretroviral therapy, or ART. For more information on ART, see CATIE's *Your Guide to HIV Treatment*.

Odefsey is a complete treatment in one pill and is meant to be used by HIV-positive adults who:

- do not have HIV that is resistant to TAF, FTC and related drugs (these are commonly called nucleoside analogues or nukes);
- do not have HIV that is resistant to rilpivirine and related non-nuke drugs such as nevirapine, efavirenz (in Atripla) and so on; and
- have levels of HIV in the blood (viral load) less than 100,000 copies/mL

Odefsey is taken once daily with a meal. Odefsey needs the fat in a meal to help ensure it is absorbed.

For many people with HIV, the use of ART has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to greatly reduce the risk of developing a life-threatening infection. Neither Odefsey nor any other anti-HIV medication is a cure for HIV. It is therefore important that you see your doctor for checkups and lab tests on a regular basis.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing undetectable viral load are substantially less likely to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load* to prevent HIV transmission). However, it is still a good idea to use condoms because they can reduce your risk for getting and passing on other sexually transmitted infections.

Warnings

Most people who take Odefsey will experience few or no problems, but some issues to be aware of include the following:

1. Mental health

In clinical trials, problems related to depressive illness occurred in some people who used rilpivirine-containing regimens, including Odefsey. Symptoms included depression, anxiety and negative thoughts. In about 5% of participants, the severity of these symptoms ranged from moderate to life-threatening.

However, only about 1% of Odefsey users in clinical trials needed to stop taking this drug because of symptoms of depressive illness. Mental health issues are relatively common in HIV infection (regardless of whether or not people are taking treatment or the type of treatment).

Some people who use Odefsey may experience problems with thoughts and feelings. For example, you may have one or more of the following:

- become easily upset or angry
- have unexpected feelings of sadness
- have prolonged feelings of sadness, anger or depression
- feel hopeless
- have loss of pleasure in everyday activities
- feel fearful
- unexpectedly feel tired or experience a lack of energy
- have difficulty falling asleep, staying asleep or waking up prematurely
- have strange thoughts
- have thoughts about harming yourself or others
- have thoughts about suicide

If you notice any of these problems before or after you have started to take Odefsey, talk to your doctor right away.

2. Cardiovascular health

The manufacturer advises that Odefsey should be used with caution in people who might have cardiovascular health conditions, including abnormal heart rhythms, heart failure, poor circulation of blood to the heart and so on. In clinical trials, researchers found that exposure to rilpivirine (one of the drugs in Odefsey) gradually affected the hearts of some volunteers so that they were more likely to develop abnormal heart rhythms.

Symptoms of abnormal heart rhythms can include the following:

- dizziness
- fainting
- heart palpitations (a feeling that your heart is pumping very hard or fast when you are at rest)
- seizures

If you develop any of these symptoms, talk to your doctor right away.

If you have cardiovascular disease, including abnormal heart rhythms, or have a parent, brother or sister with any type of heart problem, let your doctor(s) know.

3. Hepatitis and liver health

Rilpivirine (one of the drugs in Odefsey) has been tested in only a small number of people with mild-to-moderate liver injury. Therefore, the manufacturer recommends that people with severe liver injury do not use Odefsey and that it be used with caution in people with mild-to-moderate liver injury.

In some clinical trials in which HIV-positive patients who are co-infected with hepatitis B or C received rilpivirine, increased levels of liver enzymes in the blood were found. The increased levels of these enzymes were greater than in other clinical trial participants who were not co-infected with hepatitis viruses.

The manufacturer recommends lab testing of blood before starting and during therapy with Odefsey. These tests should include screening for any liver injury or disease.

Increased levels of liver enzymes may suggest liver inflammation, liver injury and dysfunction; talk to your doctor about your test results.

4. Pancreatitis

There have been reports of painfully swollen pancreas glands in some people taking tenofovir (one of the drugs in Odefsey) as part of ART. Higher-than-normal blood levels of the enzyme amylase (made by the pancreas) have been detected in people taking tenofovir. This increase may suggest inflammation in the pancreas. Symptoms of pancreatitis can include the following:

- abdominal pain, particularly when laying down
- nausea
- vomiting
- unexpected sweating
- fever
- anxiety

If any of these symptoms occur, talk to your doctor right away.

5. Pregnancy

As there is no information from large numbers of pregnant women on the safety of Odefsey for these women or their fetuses, the manufacturer recommends that Odefsey "should not be used during pregnancy unless the benefits outweigh the potential risks to the fetus."

6. Age

The manufacturer recommends that Odefsey should be used with caution in patients 65 years and older since clinical trials did not enroll sufficient people in this age group to assess its safety.

Side effects

The following is not a complete list of potential side effects; speak to your pharmacist and doctor to find out more. In some cases, researchers are not certain why some side effects occur.

1. General

Information from clinical trials suggest that Odefsey is generally well tolerated.

Here is a list of some symptoms reported by rilpivirine users in clinical trials; usually these side effects were mild and temporary:

- dizziness
- feeling sleepy during the daytime
- headache
- rash
- nausea
- stomach pain

If these or other symptoms persist or are bothersome, let your doctor know.

2. Depression (see Warnings)

Odefsey has the potential to cause depression and anxiety, although in clinical trials, less than 10% of people reported this problem. Before severe depression occurs subtle symptoms, which may possibly be related, may appear, including:

- difficulty concentrating
- problems falling asleep
- problems staying asleep
- not feeling refreshed after a night's sleep
- worrying excessively
- persistent irritability
- difficulty remembering
- unexpected fatigue
- changes in appetite
- persistent nightmares

If you notice any of these symptoms or changes to your mood, speak to your doctor right away.

3. Lactic acidosis

In very rare cases, people who have used the medicines in Odefsey have experienced a condition called lactic acidosis – higher-than-normal levels of lactic acid in the blood. Researchers are not sure why this happens. Women who are overweight are at increased risk for lactic acidosis. Sometimes the liver of a person with lactic acidosis becomes swollen because of fatty deposits.

Signs and symptoms of lactic acidosis may include the following:

- nausea
- vomiting
- abdominal pain
- diarrhea
- unexpected tiredness
- unexpected muscle pain
- feeling cold especially in the arms and legs
- feeling dizzy or light-headed

If these symptoms persist, see your doctor right away.

4. Bone health

Odefsey contains tenofovir in the form of TAF. Clinical trials have found that TAF is generally safer for the kidneys and bones than the older form of tenofovir (tenofovir DF). Bear in mind that some people with HIV can develop thinner-than-normal bones without ever using medicines. Studies have found that after starting ART, some people may have their bone density decrease. The decrease in bone density tends to stabilize within one or two years after starting ART. It may be useful for you to discuss with your doctor the possibility of having bone density assessments done before you begin taking Odefsey or any other anti-HIV therapy. If your bones are thin, talk to your doctor about your intake of calcium and vitamin D_3. Regular

monitoring of bone density may also be useful for some people.

For more information about vitamin D and bones, see CATIE's *A Practical Guide to a Healthy Body for People Living with HIV* and *A Practical Guide to HIV Drug Side Effects*.

5. Kidney health

Odefsey contains TAF (a form of tenofovir), which is removed from the body by the kidneys and put into urine. Kidney injury does not commonly occur in people who use TAF. The manufacturer recommends that doctors screen patients for kidney problems before starting therapy with Odefsey. Having regular blood and urine tests done while you are taking Odefsey can help your doctor assess your kidney health. Some of the tests used to assess kidney health include the following:

- creatinine
- e-GFR (estimated glomerular filtration rate)
- calcium
- phosphorus
- bicarbonate

6. Changes in body shape

In general, Odefsey does not cause significant changes in body shape. However, people who initiate ART generally experience a degree of weight gain (usually a few pounds or kilos) in subsequent months or years. This occurs because ART helps to improve overall health and the health of the digestive tract in particular.

Food interactions

Odefsey must always be taken with a meal so that it is absorbed.

Avoid eating grapefruit or drinking grapefruit juice because these will increase the concentration of rilpivirine in your body leading to side effects.

Drug and herb interactions

Always consult your doctor and pharmacist about taking any other prescription or non-prescription medication, including over-the-counter medicines, herbs, supplements and street drugs.

Some drugs can interact with Odefsey, increasing or decreasing the levels of the medicines in Odefsey in your body. Increased drug levels can cause you to experience side effects or make pre-existing side effects worse. On the other hand, if drug levels become too low, HIV can become drug-resistant and your future treatment options may be reduced.

If you must take a drug that has the potential to interact with your other medications, your doctor can do the following:

- adjust the dose of either your anti-HIV drugs or other medications; or
- prescribe different anti-HIV drugs.

The manufacturer warns that the following drugs and herbs should not be used with Odefsey because they can severely reduce the concentration of one or more of the drugs in Odefsey in the blood and cause HIV to become resistant to rilpivirine and other anti-HIV medications (note that the following list is not exhaustive):

- antibiotics for tuberculosis or MAC (mycobacterium avium complex) – rifabutin (Mycobutin), rifampin (Rifadin, Rofact and in Rifater), rifampicin and rifapentene
- antiseizure drugs – carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- corticosteroids – dexamethasone given as pills or by injection. High doses of corticosteroids can accumulate in the body and interact with rilpivirine.
- herbs – St. John's wort (hypericin, hyperforin)
- proton pump inhibitors – dexlansoprazole (Dexilant), esomeprazole (Nexium), lansoprazole (Prevacid), omeprazole (Losec), pantoprazole (Pantoloc), rabeprazole (Pariet)

The manufacturer warns that the following drugs should not be used with Odefsey because they can

greatly increase levels of rilpivirine (one of the drugs in Odefsey) and can cause side effects:

- non-nukes – efavirenz (Sustiva, also in Atripla), etravirine (Intelence), nevirapine (Viramune) and delavirdine (Rescriptor)

The manufacturer warns that the following drugs can change levels of rilpivirine and/or other drugs in Odefsey and suggests that physicians exercise caution when prescribing these drugs to patients who are taking Odefsey:

- antacids containing aluminum, magnesium hydroxide or calcium carbonate. These drugs should be used with caution as they can affect the acidity of the stomach and greatly decrease absorption of rilpivirine and reduce its levels in the blood. The manufacturer recommends that antacids should only be used "either at least two hours before or at least four hours after Odefsey."
- antifungal agents – fluconazole (Diflucan), ketoconazole, itraconazole (Sporanox), posaconazole (Spirafil) and voriconazole (Vfend). These can all increase levels of rilpivirine and TAF in the blood and rilpivirine in turn can reduce the concentration of these drugs, which can lead to new or recurring fungal infections.
- HIV protease inhibitors – atazanavir (Reyataz), darunavir (Prezista), fosamprenavir (Telzir), lopinavir-ritonavir (Kaletra), ritonavir (Norvir), saquinavir (Fortovase), tipranavir (Aptivus).

The following drugs can increase rilpivirine levels:

- macrolide antibiotics – clarithromycin (Biaxin), erythromycin and troleandomycin can all increase rilpivirine levels and lead to side effects. The manufacturer suggests that where possible, physicians consider the use of an alternative macrolide, such as azithromycin (Zithromax).

The following drugs can decrease rilpivirine levels and must be used with caution:

- histamine$_2$-receptor antagonists – cimetidine (Tagamet), famotidine (Pepcid), nizatidine, ranitidine (Zantac). These drugs reduce the acidity of the stomach and can therefore significantly reduce the absorption of rilpivirine. This can lead to HIV becoming resistant to rilpivirine and other anti-HIV drugs. The manufacturer suggests that these drugs should be used with caution and if they must be used, they should only be taken "at least 12 hours before or at least four hours after Odefsey."

The transplant drug cyclosporine (Neoral, Sandimmune) can increase levels of TAF in the body.

Other drugs

Odefsey may interact with some treatments for hepatitis C; speak to your doctor, nurse or pharmacist to find out more.

Medicines that cause people to urinate excessively (such as water pills or diuretics) or have diarrhea (laxatives or enemas), or other drugs such as amphotericin B (Fungizone, Abelcet) can upset the balance of minerals in your blood and could affect your heart's rhythm. The manufacturer recommends that such drugs be used with caution in people taking Odefsey.

Interactions are not expected

The manufacturer does not expect the drugs inside Odefsey to interact with these drugs:

- methadone
- HIV and hepatitis drugs—maraviroc (Celsentri), raltegravir (Isentress), and nukes for hepatitis C treatment, such as ribavirin
- erectile dysfunction drugs, such as sildenafil (Viagra), tadalafil (Cialis) or vardenafil (Levitra)
- lipid-lowering agents, called statins, including atorvastatin (Lipitor), rosuvastatin (Crestor) and similar drugs
- oral contraceptives ("the pill")

Resistance, cross-resistance and treatment interruption

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes are called mutations and can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you. Combining rilpivirine with at least two other anti-HIV drugs, as Odefsey does, delays the development of drug resistance.

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed. If doses are delayed, missed or not taken as prescribed, blood levels of the drugs in Odefsey may fall too low. If this happens, resistant virus can develop. If you are having problems taking your medications as directed, speak to your doctor and nurse about this. They can find ways to help you.

When HIV becomes resistant to one drug in a class, it sometimes becomes resistant to other drugs in that class. This is called cross-resistance. Feel free to talk with your doctor about your current and future treatment options. To help you decide what these options might be, your doctor can have a small sample of your blood analyzed using resistance testing. Should HIV in your body become resistant to rilpivirine, your doctor can recommend a new drug combination for you.

Dosage and formulations

Odefsey is available as purplish-pink tablets. Each tablet contains the following medications:

- rilpivirine – 25 mg
- FTC – 200 mg
- TAF – 25 mg

The adult dose is one tablet taken once daily with a meal.

Availability

Odefsey is licensed in Canada for the treatment of HIV infection in adults who have never used antiretroviral drugs. Your doctor can tell you more about the availability and coverage of Odefsey in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

References

Gilead Sciences. Odefsey (emtricitabine/rilpivirine/tenofovir alafenamide tablets). *Product monograph*. 21 February, 2017.

Gilead Sciences. Complera (emtricitabine/rilpivirine/tenofovir disoproxil fumarate tablets). *Product monograph*. 7 June, 2017.

Cohen CJ, Andrade-Villanueva J, Clotet B, et al. Rilpivirine versus efavirenz with two background nucleoside or nucleotide reverse transcriptase inhibitors in treatment-naive adults infected with HIV-1 (THRIVE): a phase 3, randomised, non-inferiority trial. *Lancet*. 2011 Jul 16;378(9787):229–37.

Orkin C, DeJesus E, Ramgopal M, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide coformulated with rilpivirine and emtricitabine in virally suppressed adults with HIV-1 infection: a randomised, double-blind, multicentre, phase 3b, non-inferiority study. *Lancet HIV*. 2017 May;4(5):e195–e204.

Mocroft A, Kirk O, Reiss P et al. Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients. *AIDS*. 2010 Jul 17;24(11):1667–78.

Molina JM, Cahn P, Grinsztejn B et al. Rilpivirine versus efavirenz with tenofovir and emtricitabine in treatment-naive adults infected with HIV-1 (ECHO): a phase 3 randomised double-blind active-controlled trial. *Lancet*. 2011 Jul 16; 378(9787):238–46.

Wilkin A, Pozniak A, Morales-Ramirez J et al. Long-term efficacy, safety, and tolerability of rilpivirine (RPV, TMC278) in HIV Type-1-infected antiretroviral-naïve patients: Week 192 results from a phase IIb randomized trial. *AIDS Research and Human Retroviruses*. 2012 May;28(5):437–46.

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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