

# Hepatitis C treatment factsheet

## **Viekirax (paritaprevir/ombitasvir/ritonavir) and Exviera (dasabuvir)**

*Viekirax* and *Exviera* are two new medications used to treat hepatitis C. *Viekirax* is a combination pill containing paritaprevir and ombitasvir with a booster dose of ritonavir. *Exviera* or dasabuvir is a separate pill usually taken with *Viekirax*.

*Viekirax* and *Exviera* were approved in Europe in January 2015 for treatment of adults with genotype 1 chronic hepatitis C. Most people should take these medications with ribavirin. *Viekirax* without *Exviera* was also approved for people with genotype 4 hepatitis C. In Europe, *Viekirax* and *Exviera* are available for separate prescription, but in some countries they are packaged together (*Viekira Pak* in the US and Australia, *Holkira Pak* in Canada).

The *Viekirax* and *Exviera* regimen offers a new interferon-free option for many people with hepatitis C. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

### How do *Viekirax* and *Exviera* work?

*Viekirax* contains two direct-acting antiviral drugs that target different steps of the hepatitis C virus (HCV) lifecycle. Paritaprevir is an HCV protease inhibitor, meaning it blocks the protease enzyme which the virus needs to reproduce. It is combined with a small dose of ritonavir to boost its level in the blood. Ombitasvir is an HCV NS5A replication complex inhibitor that interferes with another important HCV protein. *Exviera* or dasabuvir is a non-nucleoside HCV polymerase inhibitor that blocks a third viral enzyme. Targeting multiple steps of the HCV lifecycle makes the combination more effective and makes it harder for the virus to develop drug resistance.

### Who can use *Viekirax* and *Exviera*?

*Viekirax* and *Exviera* are indicated for use by adults with chronic hepatitis C, meaning infection lasting more than six months. *Viekirax* plus *Exviera*, taken with or without ribavirin, were approved for people with HCV genotype 1. Genotype 1 is the most common type in Europe. *Viekirax* without *Exviera* was approved for use with ribavirin for people with HCV genotype 4.

*Viekirax* and *Exviera* can be used by people being treated for hepatitis C for the first time (known as ‘treatment-naive’) and for retreatment of people who were not cured with previous interferon-based therapy (known as ‘treatment-experienced’).

*Viekirax* and *Exviera* have been tested in people with HIV and HCV co-infection. Response rates and side-effects are similar to those of HIV-negative people, but some of the drugs in this combination can interact with antiretroviral medications for

HIV. People with HIV and HCV co-infection who want to take this regimen should do so under the care of a doctor who has experience treating both infections.

*Viekirax* and *Exviera* can be used by people with all stages of compensated liver disease including cirrhosis. However, it works better for people with less advanced liver damage. This combination must not be used by people with advanced or decompensated cirrhosis or severe liver function impairment, but it can be used by people who have recurring HCV infection after a liver transplant.

*Viekirax* and *Exviera* can be used by people using opioid substitution therapy, such as methadone or buprenorphine, to manage drug addiction.

### How are *Viekirax* and *Exviera* taken?

*Viekirax* is taken as two tablets once daily (in the morning) with food. *Exviera* is taken as a one tablet twice daily (in the morning and evening) with food. Most people will also need to take ribavirin pills twice daily, with doses based on body weight. Recommended combinations and length of treatment will depend on a person’s HCV genotype and amount of liver damage. Genotype 1 includes two subtypes, 1a and 1b, with 1a being harder to treat.

	Combined with:	Length of treatment
<b>Genotype 1b without cirrhosis</b>	<i>Viekirax</i> + <i>Exviera</i>	12 weeks
<b>Genotype 1b with compensated cirrhosis</b>	<i>Viekirax</i> + <i>Exviera</i> + ribavirin	12 weeks
<b>Genotype 1a without cirrhosis</b>	<i>Viekirax</i> + <i>Exviera</i> + ribavirin	12 weeks
<b>Genotype 1a with compensated cirrhosis</b>	<i>Viekirax</i> + <i>Exviera</i> + ribavirin	24 weeks
<b>Genotype 4 without cirrhosis</b>	<i>Viekirax</i> + ribavirin	12 weeks

	Combined with:	Length of treatment
<b>Genotype 4 with compensated cirrhosis</b>	<i>Viekirax</i> + ribavirin	24 weeks

All people without liver cirrhosis can be treated for 12 weeks, but those with genotype 1a or 4 who have compensated cirrhosis should extend treatment to 24 weeks. People with genotype 1b and no cirrhosis do not need ribavirin. *Exviera* does not work against genotype 4, so people with this genotype should take *Viekirax* with ribavirin alone.

Recommendations for people with HIV and HCV co-infection are the same as for HIV-negative people. However, *Viekirax* should not be used with certain antiretroviral medications. *Viekirax* contains ritonavir and should not be combined with additional ritonavir used to boost HIV protease inhibitors. People with HIV and HCV co-infection who are not on antiretroviral therapy should not use *Viekirax* because the ritonavir could cause HIV drug resistance.

Liver transplant recipients with HCV genotype 1 should use *Viekirax* and *Exviera* plus ribavirin for 24 weeks. Ribavirin doses may need to be lowered to reduce side-effects.

*Viekirax* and *Exviera* are not approved for people with HCV genotypes 2, 3, 5 or 6.

## How effective are *Viekirax* and *Exviera*?

*Viekirax* and *Exviera* work better for some people than for others. Several factors predict how well someone will respond, including HCV genotype, extent of liver damage and previous treatment history.

People with advanced liver disease do not respond as well as those with mild or moderate liver fibrosis. People who are new to treatment have a better chance of being cured than those who did not respond to prior treatment. These factors may be overcome by longer treatment or by adding ribavirin, which helps prevent relapse.

Other factors that traditionally predict poor response to interferon-based therapy do not make as much difference with interferon-free treatment.

## *Viekirax* and *Exviera* treatment response

The safety and effectiveness of *Viekirax* and *Exviera* (also known as the '3D' regimen) were tested in more than 2300 people with chronic hepatitis C in six large international clinical trials.

Overall, 90% to 100% of study participants with HCV genotype 1 were cured using *Viekirax* plus *Exviera*, with or without ribavirin, for 12 or 24 weeks. People with sustained virological

response, who still have undetectable HCV viral load 12 weeks after finishing treatment (known as 'SVR12'), are considered cured.

The SAPPHERE-I and -II trials showed that *Viekirax* plus *Exviera* with ribavirin for 12 weeks cured 96% of previously untreated and treatment-experienced people with HCV genotype 1 without cirrhosis, including a majority with harder-to-treat subtype 1a.

The PEARL-II and -III studies compared 12 weeks of *Viekirax* plus *Exviera* with or without ribavirin for treatment-naive and treatment-experienced people with easier-to-treat genotype 1b without cirrhosis, while PEARL-IV looked at previously untreated people with genotype 1a. Everyone with genotype 1b was cured with *Viekirax* plus *Exviera* without ribavirin. For those with genotype 1a cure rates were 90% without ribavirin and 97% with ribavirin.

The TURQUOISE-II trial showed that *Viekirax* plus *Exviera* with ribavirin for 12 weeks cured 99% of previously untreated and treatment-experienced people with genotype 1b who had compensated cirrhosis with mild liver function impairment. Among people with genotype 1a, the cure rate was 95% with 24 weeks of treatment. Side-effects were similar to those seen in people without cirrhosis.

The smaller TURQUOISE-I study showed that *Viekirax* plus *Exviera* with ribavirin for 12 or 24 weeks cured 92% of people with HIV and HCV co-infection (mostly with HCV subtype 1a). The CORAL-I study saw a cure rate of 97% for genotype 1 liver transplant recipients who took *Viekirax* plus *Exviera* with ribavirin for 24 weeks. The cure rate was also 97% in a small study of people on opioid substitution therapy.

*Viekirax* plus ribavirin without *Exviera* (also known as the '2D' regimen) cured 100% of treatment-naive and treatment-experienced people with HCV genotype 4 in the PEARL-I study, but the response rate fell to 91% without ribavirin.

The effectiveness of *Viekirax* and *Exviera* in 'real world' use may be somewhat lower than cure rates seen in clinical trials, in part because patients may be sicker or have other conditions that make treatment more complicated.

## What are the side-effects of *Viekirax* and *Exviera*?

The drugs in *Viekirax* and *Exviera* are generally safe and well tolerated. The most common side-effects seen in clinical trials were fatigue, nausea, insomnia, weakness and itching. Ribavirin can cause side-effects including anaemia (low haemoglobin level). Participants in the SAPPHERE trials who took *Viekirax* and *Exviera* with ribavirin were no more likely to stop treatment due to side-effects than those taking inactive placebo pills.

*Viekirax* and *Exviera* have not yet been tested in pregnant or breastfeeding women. Ribavirin can cause birth defects, so it should not be used by pregnant women, women planning to become pregnant, or their male partners.

## Do *Viekirax* and *Exviera* interact with other drugs?

The drugs in *Viekirax* and *Exviera* can interact with other drugs that are processed by the same enzymes in the liver or intestines. These include some antiretroviral drugs for HIV, contraceptive pills, allergy medications, antibiotics, TB medications, statins and other heart drugs, psychiatric medications and herbal products containing St John's wort. Sometimes drug doses can be adjusted to overcome these interactions, but some medications should not be used together with *Viekirax* and *Exviera*. Information about specific drug interactions is available online at [www.hep-druginteractions.org](http://www.hep-druginteractions.org).

## How can I get *Viekirax* and *Exviera*?

*Viekirax* and *Exviera* are available by prescription in European Union countries to treat people with hepatitis C genotypes 1 or 4, subject to national approval. When to start treatment will depend on a number of factors, including severity of liver damage (as determined by *FibroScan* or a liver biopsy). Ask your GP or liver specialist if *Viekirax* and *Exviera* may be a good option for you.

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This information is intended to support, rather than replace, consultation with a healthcare professional. Talk to your doctor or another member of your healthcare team for advice tailored to your situation.

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