infohep

News and information on viral hepatitis in Europe

Hepatitis C treatment factsheet
Daclatasvir (*Daklinza*)

Daclatasvir (brand name *Daklinza*) is a new medication used to treat hepatitis C. It was approved in Europe in August 2014 for treatment of adults with chronic hepatitis C genotypes 1, 2, 3 or 4.

For some people, daclatasvir can be used in interferon-free regimens with other oral hepatitis C medications. For others, daclatasvir can shorten treatment when added to pegylated interferon and ribavirin. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

How does daclatasvir work?

Daclatasvir is one of the new direct-acting antiviral drugs that target different steps of the hepatitis C virus (HCV) lifecycle. It is the first-ever approved HCV NS5A replication complex inhibitor, meaning it interferes with a protein the virus uses to reproduce.

Daclatasvir should be combined with other medications, which may include other direct-acting antivirals that work differently – such as the HCV polymerase inhibitor **sofosbuvir (*Sovaldi*)** or the HCV protease inhibitor asunaprevir (*Sunvepra*) – or pegylated interferon and ribavirin.

Who can use daclatasvir?

Daclatasvir is indicated for use by adults with chronic hepatitis C, meaning infection lasting more than six months. It is approved for people with HCV genotype 1, 2, 3 or 4. Genotype 1 is the most common type in Europe and considered the hardest to treat.

Daclatasvir 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').

The safety and effectiveness of daclatasvir for people with HIV and HCV co-infection has not yet been determined, but this is now being tested. Studies have shown that daclatasvir does not have problematic interactions with most widely used HIV drugs. People with HIV and HCV co-infection who want to take daclatasvir should do so under the care of a doctor who has experience treating both HIV and HCV.

Daclatasvir 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. Daclatasvir is now being tested for people with chronic hepatitis C who are awaiting or have received liver transplants.

How is daclatasvir taken?

Daclatasvir is available in 30 and 60mg tablets, and the usual dose is 60mg once daily with or without food. It must be used in combination with other hepatitis C medications and is not effective if taken alone. Treatment should be managed by a doctor who has experience treating hepatitis C.

	Combined with:	Length of treatment
Genotype 1	Daclatasvir & sofosbuvir	12 weeks (no cirrhosis) 24 weeks (with cirrhosis)
Genotype 1	Daclatasvir & sofosbuvir & ribavirin	12 weeks (post-liver transplant, no cirrhosis) 12 weeks (with cirrhosis A or B) 24 weeks (with decompensated cirrhosis)
Genotype 2	Daclatasvir & sofosbuvir	Evidence lacking to make a recommendation on duration; at least 12 weeks.
Genotype 3	Daclatasvir & sofosbuvir	12 weeks (no cirrhosis)
Genotype 3	Daclatasvir & sofosbuvir & ribavirin	12 weeks (post-transplant, no cirrhosis) 24 weeks (with cirrhosis)
Genotype 4	Daclatasvir & sofosbuvir	12 weeks (no cirrhosis) 24 weeks (with cirrhosis)
Genotype 4	Daclatasvir & sofosbuvir & ribavirin	12 weeks (post-transplant or with cirrhosis A or B) 24 weeks (with decompensated cirrhosis)

Daclatasvir plus weekly pegylated interferon injections and ribavirin pills for 24 weeks is another option for people with genotype 4. Slow responders should continue on pegylated interferon and ribavirin for 48 weeks.

How effective is daclatasvir?

Daclatasvir works 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 liver cirrhosis do not respond as well as those with mild or moderate liver fibrosis. Depending on which drugs daclatasvir is combined with, people who are new to treatment may have a better chance of being cured than those with little or no response to prior treatment.

However, factors that traditionally predict poor response to interferon-based therapy do not make as much difference with interferon-free treatment. These factors may be overcome by prolonging treatment or by adding another direct-acting antiviral or ribavirin.

Daclatasvir treatment response

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

A phase 2 study (AI444040) looked at people with HCV genotype 1, both previously untreated and those already treated with pegylated interferon and ribavirin plus the older HCV protease inhibitors boceprevir (*Victrelis*) or telaprevir (*Incivo*). Daclatasvir plus sofosbuvir cured 100% of people in both groups treated for either 12 or 24 weeks.

Daclatasvir plus sofosbuvir for 24 weeks was also tested in a smaller number of previously untreated people with HCV genotype 2 or 3. Daclatasvir plus sofosbuvir alone cured 96% of people with genotype 2 and 89% of those with genotype 3. Adding ribavirin brought the cure rate for genotype 3 up to 100% as well.

In the COMMAND-4 trial (AI444042) daclatasvir was tested in combination with pegylated interferon and ribavirin for previously untreated people with HCV genotype 4. About 80% of people with or without cirrhosis were cured with the triple combination – more than twice as many as those taking interferon and ribavirin alone.

Daclatasvir's effectiveness 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 daclatasvir?

Daclatasvir is generally well tolerated with no known specific side-effects of its own. The most common side-effects seen in people taking daclatasvir with sofosbuvir are fatigue, nausea and headache.

Taking daclatasvir with interferon and ribavirin can lead to additional side-effects including fever, muscle and joint aches, itching, depression, anaemia (low haemoglobin level) and neutropenia (low white blood cell count). Ribavirin can also cause birth defects, so it should not be used by pregnant women or their male partners.

Does daclatasvir interact with other drugs?

Daclatasvir can interact with other drugs that are processed by the same enzymes in the liver and intestines. These include some antibiotics, TB medications, anti-seizure drugs 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 daclatasvir. Information about specific drug interactions is available online at www.hep-druginteractions.org.

How can I get daclatasvir?

Daclatasvir is available by prescription in several European Union countries to treat genotype 1, 2, 3 and 4 hepatitis C. Ask your GP or liver specialist if daclatasvir is available in your country and if it may be a good option for you.

When to start treatment will depend on a number of factors, including severity of liver damage (as determined by *FibroScan* or a liver biopsy). People with mild liver disease may be able to wait, and more new hepatitis C medications that can be used in interferon-free treatment are coming soon. However, the decision to wait must take into account how fast your liver disease might progress – which is hard to predict – and how soon these new treatments will be approved in your country.

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