



HCSP FACT SHEET

• HCV TREATMENT: GENERAL INFORMATION •

Prescription Drugs – Off-label Use

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Foreword

Medications that are approved by the Food and Drug Administration (FDA) go through a vigorous clinical development process to find out if the drug is safe and effective in treating a specific condition. The pharmaceutical company will compile the data from one or more Phase 3 studies and submit it to the FDA. If the medications are approved the pharmaceutical company will develop a package label that is used by medical providers. The package label is also called the prescribing information.

Prescribing Information

The prescribing information includes the dosage(s) of the medications, when to take the medication, what, if any, food requirements to take or avoid, the duration of the treatment, side effects including the more severe side effects, important warnings about the drug, who should not take the drug, and additional important information. This information should be read by medical providers, patients and patient advocates.

The FDA will review the label put together by the pharmaceutical company, make recommendations or changes to the label, and once all parties agree, will authorize the drug for use. After the drug has been used by a large population with the condition, other uses of the drug may come to light. This can happen after research into the benefits of the drug or it may come about by accident when a person has a condition for which the drug seems to have a positive effect. For example, a drug was being tested to treat depression, but during the development process it was also found to help with insomnia. A medical provider may decide to prescribe it for a patient with insomnia “off label.” It may turn out that there is such a need for the drug used off-label that the pharmaceutical company may decide to study the drug for this other condition. Off-label use has many benefits, but it could also be dangerous.

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The information in this fact sheet is designed to help you understand and manage HCV and is not intended as medical advice. All persons with HCV should consult a medical practitioner for diagnosis and treatment of HCV.

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Prescription Drugs – Off-label Use

Most people would be surprised at the amount of drugs that are prescribed off-label. A recent report found that 1 in 5 prescriptions were prescribed off-label. Many doctors and most patients, however, are not aware that the drug they are being prescribed is off-label use. Unlike FDA approval, off-label use is not regulated, but it is legal for a medical provider to prescribe off-label. Pharmaceutical companies, however, can't promote the off-label use without facing stiff fines by the FDA.

Below are but a few of the off-label uses for certain approved medications:

- Propranolol (Inderal), approved for high blood pressure and heart disease, but used off-label for stage fright.
- Mirtazapine (Remeron), approved to treat major depressive disorder, but used off-label to treat insomnia.
- Amitriptyline (Elavil), approved to treat depression, but used off-label to treat fibromyalgia and migraines.

Health Risks

Off-label use has the potential to cause serious harm and even death from some drugs used 'off-label.' There may be unforeseen drug-drug interactions or the drug may exacerbate an already serious condition like liver disease. The drugs may also be harmful to certain populations like children or the elderly. The off-label use of a drug could potentially lead to the development of drug resistance.

Benefits

There are many benefits to having the opportunity to use drugs off-label. They may be used to treat a condition that has few treatment options. This is particularly relevant to cancer patients who have

limited approved treatment options and off-label use can save lives for those who can't wait for clinical studies and FDA approval.

Prescription Drug Coverage

Medications that are being used off-label may not be covered by medical insurance, which may be too expensive for many people.

The Future

There are many medical professionals who are calling for more regulations to govern off-label use. But at the same time it is important to recognize that over-regulation can hinder innovation and deny life-saving drugs to people who have very few options.

Important Questions to Ask

If you are being prescribed a medication talk with your medical provider:

- Ask your medical provider if the drug he or she is prescribing is FDA approved or if it is being prescribed off-label.
- Read the FDA approved package label—your medical provider and/or pharmacist can give you a copy. The [HCV Advocate](#) and [HBV Advocate](#) websites have the package label in the treatment sections for FDA approved HBV and HCV medications.
- Ask if the off-label drug provides more benefits than the approved medication.
- Ask your medical provider why he or she is prescribing the drug off-label.
- Ask if the risks and benefits justify off-label use.
- Check with your insurance company to find out if your insurance covers the off-label drug; what are the co-pays; what are the deductibles.

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- Check with a pharmacist about possible drug-drug interaction—they are experts.

HCV and Off-Label Use

Off-label use of pegylated interferon and HCV protease inhibitors is already occurring. But since only one class (HCV protease inhibitors) is currently used the potential for harm is relatively low. However, as more HCV inhibitors are FDA approved there is a real possibility that serious harm could result from using an HCV inhibitor therapy off-label. The dose or duration of treatment could lead to drug resistance. There is also the issue of possible drug-drug interactions.

The good news in HCV drug development is that there are many companies that have and are collaborating on HCV drug development. So far, there have only been Phase 1 and Phase 2 studies. There have not been any collaborative Phase 3 studies that could lead to FDA approval. This is due to the pharmaceutical companies deciding to concentrate on their in-house drug pipelines. However, the Phase 1 and Phase 2 studies have addressed many of the important issues of off-label use including drug-drug interactions, safety and efficacy. This information can help medical providers feel more comfortable with prescribing the combination of drugs to certain patients who have not responded to the FDA-approved medications.

Some people might not want to be treated with drugs that have not been approved to treat a certain condition. Check with your medical provider to find out if a medication is being used off-label.

Cross-Company Collaborations

Gilead (sofosbuvir) and BMS (daclatasvir)

A small Phase 2 study of HCV genotype 1 (126 patients) and genotype 2 or 3 (44 patients) were treated for 12 or 24 weeks with the combination of 2 HCV polymerase inhibitors (daclatasvir and sofosbuvir) with and without ribavirin. The genotype 1 patients achieved cure rates of 96 to 98%, while genotype 2 and 3 patients achieved cure rates of 93%.

Gilead (sofosbuvir) and Janssen (simeprevir)

The Phase 2 trial included HCV genotype 1 patients who were treated with sofosbuvir and simeprevir (HCV protease inhibitor) with and without ribavirin for 12 weeks. There were two cohorts. The first cohort included treatment-naïve and null-responder patients who were staged at F-0 and F-1 (no or minimal liver disease). The interim top-line results reported cure rates 4-weeks post treatment of 93 and 96%. The second cohort included patients who were F-3 (fibrosis) and F-4 (compensated cirrhosis) and interim findings of 96% and 100% cure rates.

There are many other on-going collaborations including:

- Simeprevir, daclatasvir and VX-135 for treatment of treatment-naïve and prior null-responders.
- Daclatasvir and VX-135 for the treatment of HCV genotype 1 treatment-naïve patients.
- PPI-668, BI 207127, Faldaprevir with and without ribavirin to treat HCV genotype 1a treatment-naïve patients while on treatment.

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Related publications:

- **Patient Assistance Programs**
www.hcvadvocate.org/hepatitis/factsheets_pdf/Patient_Assistance.pdf

For more information

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| <ul style="list-style-type: none">• American Association for the Study of Liver Diseases
www.aasld.org• Centers for Disease Control and Prevention
www.cdc.gov | <ul style="list-style-type: none">• Food and Drug Administration (FDA):
www.fda.gov• Mayo Clinic
www.mayoclinic.com |
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Visit our websites to learn more about viral hepatitis:

www.hcvadvocate.org • www.hbvadvocate.org
www.hepatitistattoos.org

