# Pan-Genotypic Drugs

*An explanation of pan-genotypic drugs used to treat hepatitis C; this article originally appeared in the HCV Advocate, mid-month November 2015*

January 18, 2016 By Alan Franciscus

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In this article, I will discuss pan-genotypic drugs. I will begin with a brief discussion of hepatitis C (HCV) genotypes, a definition of pan-genotypic drugs, why they have emerged as an important part of treatment, what pan-genotypic drugs are approved and ones in the pipeline to treat HCV.

1. **Genotypes** – There are seven genotypes—numbered 1 through 7—although some experts believe there may be as many as 11 genotypes. The difference in the genotypes is due to a 1/3 difference in the genetic makeup of the HCV virus. The most common genotype worldwide and in the United States is genotype 1. Genotype 3 is the second most common in the U.S. followed by genotype 2. Genotypes 4, 5 and 6 account for less than 1% of HCV the U.S. population. There have been only four people identified with genotype 7—one person—an immigrant in Canada from the Democratic Republic of the Congo and three other people who live in the Democratic Republic of the Congo.
2. **Pan-genotype Drugs** – These are drugs that work against every genotype. The drugs may not have the same amount of antiviral activity against every genotype. For instance, one pan-genotypic drug may have a high rate of antiviral activity against genotype 1, but have a low level of antiviral activity against genotype 3. There will need to be clinical trials conducted to find out how well a particular drug works on every genotype. Most likely there will be a combination of different types of HCV inhibitors combined with the pan-genotypic drugs and different treatment durations because of the different levels of antiviral activities of the drugs.
3. **The Future** – Pan-genotypic drugs are the next leap forward in the treatment of hepatitis C. This is for many reasons. As stated above they can be combined with other drugs to treat many different genotypes.We know that some people have multiple genotypes.This is an area that needs much more research, but it is believed that about 5% to 25% of people have multiple genotypes. This can happen if people received blood transfusions before the blood products and organ transplants were screened for hepatitis C,and in people who inject drugs who share needles and works, and have multiple exposures. Treating hepatitis C with pan-genotypic drugs will treat these multiple genotypes.
4. **Current Pan-genotypic Drugs** – Sofosbuvir and daclatsavir are examples of current drugs that are FDA approved that are in fact pan-genotypic drugs. While they are active against all genotypes, they work better against some genotypes more than others. That is the main reason they are combined with other direct acting antiviral drugs.
5. **Pan-genotypic Pipeline** – There are currently two combinations that are under review by the Food and Drug Administration for marketing approval. The combination of sofosbuvir plus velpatasvir—formerly GS-5816 (with and without ribavirin) has cure rates from 80% to 100% in genotypes 1 to 6. Merck's combination of grazoprevir plus elbasvir is expected to be approved in January 2016 to treat genotypes 1,4 and 6 – the cure rates from the phase 3 clinical trials were

92% to 99%. There are many pan-genotypic drugs in development. Janssen, Achillion, and Johnson and Johnson are collaborating on various drug combinations that include pan-genotypic drugs. AbbVie and Enanta are also developing a combination of two drugs (including a pan-genotypic drug) to treat hepatitis C. The future of hepatitis C has never been more promising in HCV drug development. The only dark cloud is the price and subsequent access to treatment. Hopefully,as more drugs become available, the prices will come down so that everyone will have access.

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