Hepatitis C virus is a chronic infection that often goes undetected and can exacerbate liver diseases such as cirrhosis and liver cancer. Despite recent advances in the treatment of hepatitis C virus, the new drugs are costly and not reaching the populations most in need of the treatment. We screened a library of approved drugs and showed that a class of compounds called antihistamines – used to relieve allergies – demonstrated high anti-viral activity against the hepatitis C virus. Antihistamines are widely available, safe, and inexpensive, making them ideal for repurposing to treat hepatitis C infection and applying to low-income hepatitis C-endemic countries in Asia and Africa.