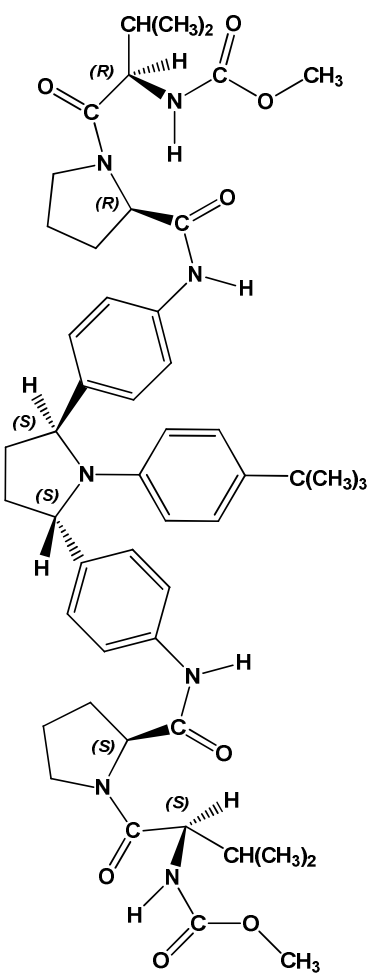
VIEKIRA PAK™ AND THE HEPATITIS C PHARMACEUTICAL MARKET



OMBITASVIR

On Friday, December 19 (2014), the Food and Drug Administration, approved Viekira pak™, a package containing four different drugs for the treatment of hepatitis C genotype 1. Viekira pak™ is marketed by the pharmaceutical company AbbVie, whose headquarters is in Chicago, Illinois, United States.

Express Script, the main manager of US prescriptions, said it will give funding for the use of this new pharmaceutical preparation to all patients, to the detriment of the two other drugs for hepatitis C (Sovaldi® [1] and Harvoni® [2, 3, 4]) by the rival company, Gilead Sciences. Unlike what occurs with Sovaldi® and Harvoni®, the two drugs by Gilead Sciences, whose funding was subject to very restrictive criteria, the authorization requirements of the new AbbVie drug will allow the drug to reach more than 25 million patients in the US alone. To achieve this, Express Script and AbbVie have negotiated a discount and special prescription conditions.

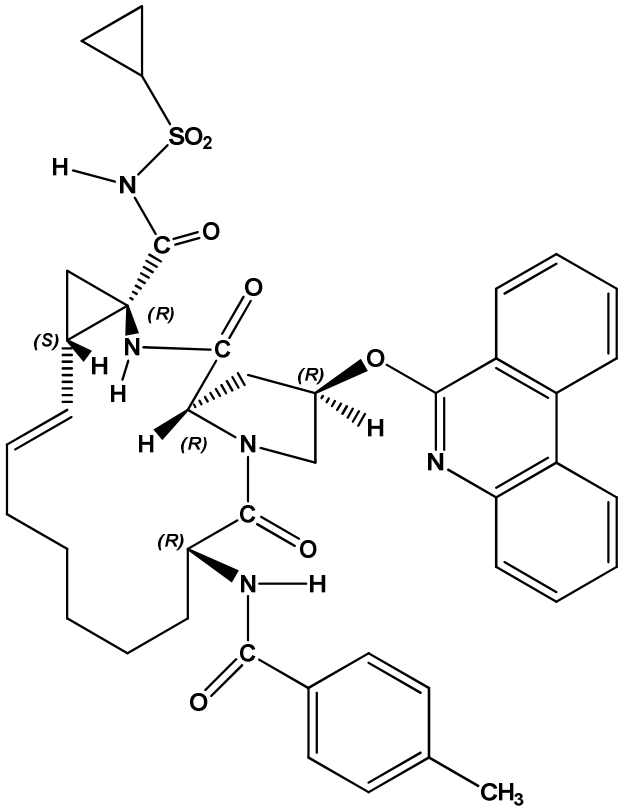
Gilead Sciences drugs have a price that many experts and patient organizations consider "outrageous"; a 12-week treatment with Sovaldi® costs $84,000, and a 12-week treatment with Harvoni® requires an outlay of $94,500.

Gilead Sciences said that the price of their drugs reflects their “real” value in curing hepatitis C. However, some state programs such as Medicaid, and the health programs of American prisons fully recognize that they cannot afford these drugs on their annual budgets. And so, the treatment with these drugs is limited to the most severe patients. The US Congress has launched an investigation into whether the prices are reasonable, having filed lawsuits against the manufacturer based on the Antitrust Law.

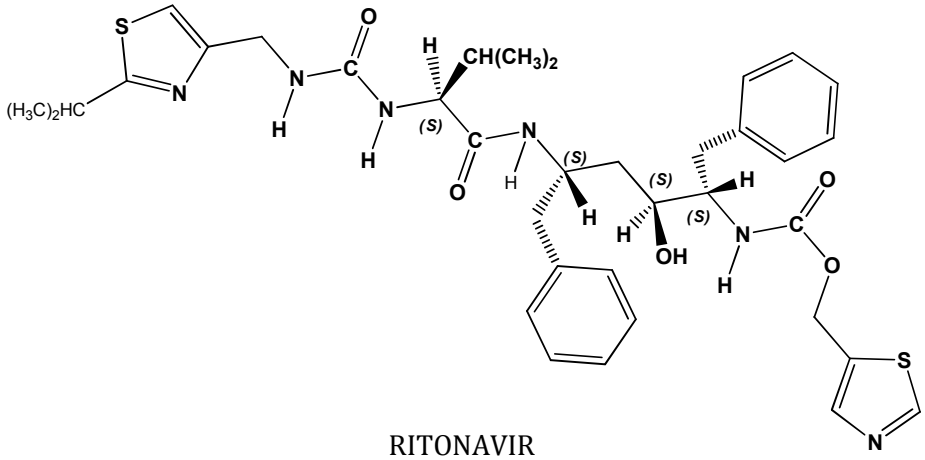
Express Scripts has gone further, promoting a boycott of Gilead Sciences drugs, especially since the marketing of Viekira pak™. However, many of the hopes for Viekira pak™ were dashed after the approval to make the cost of the new drug public by the FDA: $83,319 for a 12-week course.

Negotiations between service companies (insurance and asset management prescriptions)

and the laboratory determine the position of each drug in the Formulary, which is essential to establish which drug is used first when there are several alternatives.



PARITAPREVIR
(2*R*,6*R*,13a*S*,14a*R*,16a*R*,*E*)-*N*-(cyclopropylsulfonyl)-6-(4-methylbenzamido)-5,16-dioxo-2-(phenanthridin-6-yloxy)-1,2,3,5,6,7,8,9,10,11,13a,14,14a,15,16,16a-hexadecahydrocyclopropa[*e*]pyrrolo[1,2-*a*][1,4]diazacyclopentadecine-14a-carboxamide

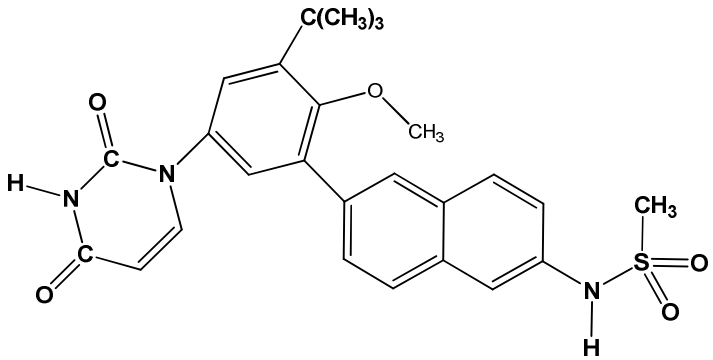


RITONAVIR
Thiazol-5-ylmethyl ((2*S*,3*S*,5*S*)-3-hydroxy-5-((*S*)-2-(3-((2-isopropylthiazol-4-yl)methyl)ureido)-3-methylbutanamido)-1,6-diphenylhexan-2-yl)carbamate

Express Script predict the exclusion of about 70 drugs next year, including Harvoni® and Sovaldi®, and the Olysio® [5, 6] , by Johnson & Johnson, which is also indicated for the

treatment of hepatitis C.

Most hepatologists declare that *all* patients with hepatitis C should be treated, regardless of the severity of their illness. However, there is some disagreement about the benefits of the Gilead Sciences drugs compared to the new AbbVie' drug (Viekira pak™). While the latter requires treatment with five daily tablets (4 in the morning and one in the afternoon), sometimes associated with Ribavirin (with significant adverse side effects), treatment with Harvoni® is much more convenient because it is in the form of a single daily tablet.



DASABUVIR
N-(6-(3-(*tert*-butyl)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-methoxyphenyl)naphthalen-2-yl)methanesulfonamide

Both Harvoni® and Viekira pak™ have been approved for hepatitis C genotype 1, responsible for approximately 70% of all cases, and patients who began treatment with Harvoni® or Sovaldi® will not be forced to take Viekira pak™ instead.

Some aspects of the negotiations between AbbVie and Express Script have been revealed, and the manufacturer and marketer (AbbVie) has said that patients requiring a 24-week course will not pay twice as much as those who only require a 12-week course, and Express Script said it will allow other medical specialists, not only hepatologists, to prescribe the drug.

Viekira pak ™ contains four drugs: Ombitavir, Paritaprevir, Ritonavir and Dasabuvir. The first three are taken at the same time in the morning (3 tablets) and Dasabuvir is to be taken twice a day.

In the European Union it has been presented as Viekirax ™ (Ombitasvir / Paritaprevir / Ritonavir) + Exviera™ (Dasabuvir). The European Commission's decision to approve the treatment is expected during the first quarter of 2015.

Viekira pak ™ is the fourth drug approved by the Food and Drug Administration after the approval of Olysio® (Simeprevir), in November 2013, followed by Sovaldi® (Sofosbuvir), in December 2013 and Harvoni® (association of Ledipasvir and Sofosbuvir), in October

2014.

The authorization by the F.D.A. was justified based on the results of six clinical trials involving 2,308 patients with hepatitis C, both cirrhotic and non-cirrhotic. All these studies included a placebo (sugar pills) group. These study groups (treated with Viekira pak®) could sometimes include treatment with Ribavirin. The treatments had a 12 or 24 weeks of duration.

The criterion of cure was «sustained viral response» (SVR) which is the non-detection of hepatitis C 12 weeks after treatment terminated. The SVR was 91%.

Treatment with Viekira pak™ consists of 3 tablets in the morning (12.5mg Paritaprevir Ombitasvir + 75mg + 50mg Ritonavir) and two daily 250mg tablets (morning and evening) of Dasabuvir.

In clinical studies, the most common side effects were fatigue, lethargy, nausea, altered sleeping pattern and itching.

Viekira pak™ is the eleventh «breakthrough therapy» drug authorized by the FDA in the last year.

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López-Tricas, JM MD
Hospital Pharmacist
Zaragoza (Spain)