

simeprevir (Olysio[°])

Chronic hepatitis C: an option for some patients

Abstract

- The choice of treatment for patients with chronic hepatitis C depends on the viral genotype and clinical situation. *Simeprevir* (Olysio[°], Janssen Cilag) inhibits the viral protease of hepatitis C virus (HCV) genotypes 1 and 4. *Simeprevir* has been authorised in the European Union for use in combination with other antivirals in adults with chronic hepatitis C.
- In HCV genotype 1 infection, two trials in treatment-naïve patients and two trials in patients in whom the *peginterferon alfa* and *ribavirin* combination had failed or who had relapsed showed that virological efficacy was enhanced when *simeprevir* was added to the *peginterferon alfa* and *ribavirin* combination. *Simeprevir* was less effective when the viral protease NS3 carried the Q80K substitution.
- An indirect comparison of the available data suggests that *simeprevir* has about the same virological efficacy as *sofosbuvir* and *boceprevir*, while a trial reported in a conference abstract suggests that it is "non-inferior" to *telaprevir*.
- Results of trials evaluating *simeprevir* without *peginterferon alfa* should be available in 2015. *Simeprevir* has not been evaluated in patients in whom triple-drug therapy has failed. Cross-resistance is likely between *simeprevir* and other viral protease inhibitors. There are no controlled trials of *simeprevir* in patients with HCV genotype 4 infection.

previr in patients with HCV genotype 4 infection.

The main known adverse effects of *simeprevir* are skin reactions (including rash and pruritus), photosensitivity, bilirubin elevation, nausea and dyspnoea. These adverse effects can be severe and even fatal. An increased risk of infections is also likely. *Simeprevir* is a substrate of P-glycoprotein and other transport proteins, as well as of cytochrome P450 isoenzyme CYP3A4, creating a risk of multiple drug interactions. *Simeprevir* bioavailability seems to be higher in patients of Asian origin, exposing them to more adverse effects and warranting the use of a lower dose.

Simeprevir is taken for 12 weeks, one tablet a day. The daily number of tablets is the same as with *sofosbuvir* and smaller than with *boceprevir* and *telaprevir*.

In practice, when triple-drug therapy is considered for chronic hepatitis C due to HCV genotype 1 but *sofosbuvir* cannot be used, *simeprevir* seems preferable to other viral protease inhibitors when the virus does not harbour the Q80K substitution. Evaluation of *simeprevir* must continue in patients in whom triple-drug therapy has failed and in patients with HCV genotype 4 infection.

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Full review available on request to subscribers. 7 pages, 24 references

POSSIBLY HELPFUL



Simeprevir is active in patients with hepatitis C due to genotype 1 strains lacking the Q80K substitution. When triple-agent therapy is warranted but *sofosbuvir* cannot be used, adding *simeprevir* to the *peginterferon alfa-ribavirin* combination increases the chances of achieving a sustained virological response. *Simeprevir* is slightly better tolerated than *boceprevir* and *telaprevir*. The efficacy of *simeprevir* on other genotypes was not known in late 2014.

Rev Prescrire 2015; 35 (376): 94-95

simeprevir capsules

OLYSIO[°]

• *Simeprevir* 150 mg per capsule

HCV antiviral; viral protease inhibitor

■ **Indication:** "In combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in adult patients". [EU centralised procedure]



In response to our request for information, Janssen Cilag provided us with administrative and published data, along with packaging items.

COMMON STEM -pamide

According to the nomenclature used to develop international nonproprietary names (INNs), established by the World Health Organization (WHO), the INNs of diuretics derived from *sulfamoylbenzoic acid* end in the common stem **-pamide** (1,2).

On 12 November 2014, the WHO list of INNs included 6 drugs of this type (1,3). Two of them are marketed in France for the treatment of hypertension: *clopamide* in a fixed-dose combination with *pindolol*; and *indapamide* used alone and in a fixed-dose combination with *perindopril* or *amlodipine* (1,3).

Note that the suffix "mide", which is not on the WHO list of common stems, is also found in the INNs of several other drugs

Translated from *Rev Prescrire* January 2015; 35 (375): 16

used in various situations (1). For example: *furosemide*, a diuretic, the sulfonylurea *glibenclamide*, the cytotoxic drug *ifosfamide*, and *lenalidomide*, a teratogenic immunosuppressant.

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Selected references from Prescrire's literature search.

- 1- World Health Organization "The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances WHO/EMP/RHT/TSN/2013.1": 135.
- 2- Prescrire Rédaction "Le suffixe du mois: -pamide" *Rev Prescrire* 1990; **10** (102): 511.
- 3- "Substance names ending with pamide", mednet.who.int accessed 12 November 2014: 1 page.

