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WHO's New Hepatitis C Drug Patent Profiles To Boost Access Worldwide

by Ian Schofield

The WHO's publication of patent analyses for new hepatitis C drugs like Sovaldi and Daklinza should make it easier for countries and generics firms to determine where generic versions can be made available.

The World Health Organization has published patent profiles for seven of the new direct acting antivirals (DAAs) for hepatitis C as part of an effort to help countries and companies identify the patent status of high-priced medicines and make generic versions available to their populations.

The WHO said the new products, which were included on the organization's essential medicines list (EML) last year, were reaching cure rates of more than 90% of people with HCV infection across different genotypes, with fewer side-effects and shorter treatment courses. Since the WHO issued its first guidelines on HCV treatment in 2014, more treatments have been approved, and it *published* updated treatment guidelines in April 2016.

But it said ensuring access to the new treatments was a "challenging task" and that for countries to identify ways of increasing access and affordability, "they need clarity about patent status." The aim of the new *working papers* on patent status, it said, was to identify the most relevant patents with respect to the medicines concerned, the countries where the patents have been filed and granted, and any secondary patents that might delay generic entry.

Ellen 't Hoen, consultant in medicines law and policy at the University Medical Centre Groningen, the Netherlands, said that patent status information had become more important now that essential medicines are more widely patented around the world.

The inclusion on the EML of new patented, highly priced medicines such as those for hepatitis C "signals that action needs to be taken by various parties to make the products affordable and available," according to 't Hoen, who was previously executive director of the Medicines Patent

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Pool.

"Patent information plays a role in that, for example negotiations about licenses and the use of compulsory licensing," and is also of interest to generic producers and suppliers in checking where they are able to market generic versions of originator drugs, she commented to the Pink Sheet. "Better information about which medicines are patented where also contributes to better policy dialogues and dialogue with industry. It provides the kind of evidence that is needed to make sound policy decisions."

The WHO has had greater transparency of patent status on its agenda since the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property was published in 2008. And its global health sector strategy on viral hepatitis for 2016-2021, which was endorsed by the World Health Assembly earlier this year, called on the organization to "advocate for comprehensive strategies to reduce prices of viral hepatitis vaccines, medicines, diagnostics and other commodities."

The new hepatitis C working papers cover the following drugs – *Gilead Sciences Inc.*'s sofosbuvir/ledipasvir (Harvoni), *Janssen Pharmaceuticals Inc.*'s simeprevir (Olsysio), *Bristol-Myers Squibb Co.*'s daclatasvir (Daklinza), and *AbbVie Inc.*'s paritaprevir, ombitasvir and dasabuvir (in combination as Viekirax + Exviera, or Viekira Pak in the US). The profiles, produced in collaboration with Thomson Reuters and Pharmathen, show the patent situation of the products in 40 individual countries, territories and regions.

According to the WHO, this will allow countries to conduct a first assessment of whether a drug is patent protected and to explore affordable treatment schemes. The profiles will also help the organization fulfil its mandate, under Resolution WHA 67.6, to assist member states in ensuring equitable access to quality, effective, affordable and safe HCV treatments, it adds.

Sofosbuvir And Daclatasvir

As for the individual patent profiles, that on sofosbuvir (Sovaldi) shows that the drug is protected by 14 different patent families, including two primary patents (a generic compound for the active metabolite of sofosbuvir, and the sofosbuvir prodrug as marketed and claiming the molecule per se in a specific compound claim), as well as crystalline forms, product-by-process and formulation patents, methods of use, processes to make sofosbuvir, and different combinations (e.g., with ledipasvir, velpatasvir and ribavirin).

While Patent 1 on sofosbuvir is not directly infringed by the manufacturing of a generic version, "it would be indirectly infringed when sofosbuvir is administered as the patent covers the active metabolite that is formed after administration of the treatment," it says. "Thus, the patent is relevant to the generic entry date. It is not listed in the USA Orange Book as only patents that protect the product as marketed are entitled to be listed in the Orange Book."

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The daclatasvir profile says a search revealed eight sponsor patents including the primary patent claiming the base compound, and secondary patents claiming formulations, methods of use, processes, product derivatives and methods for identifying NS5A-targeting compounds.

It says that the patent filing that may be "problematic to the launch of generic patents after the expiry of product patent (Patent 1) is Patent 4 [on new crystalline forms of substituted imidazole compounds]. Generic products will have to consider the expiry of patents 6 and 7 in the paritaprevir/ombitasvir/dasabuvir report, as well as their combinations. These patents by AbbVie cover combinations of at least two DAAs for treating HCV, where the treatment is either interferon-free or interferon- and ribavirin-free. These patents, together with Patent 4, should be monitored."

AbbVie's Combo

As for the paritaprevir, ombitasvir and dasabuvir combination, the profile says that in Europe paritaprevir is marketed with ritonavir and ombitasvir as Viekirax, which is given in combination with dasabuvir (Exviera), ribavirin or both. In the US, the treatment is marketed in a special pack as Viekira Pak.

It notes that the basic patents for ritonavir and ribavirin have expired and thus do not prevent their generic production. "However, patents exist on the use of ritonavir in combination with paritaprevir/ombitasvir and dasabuvir and are included in this report."

The search revealed a total of 20 patents filed by the sponsor with respect to any combination of the three new drugs, of which three are primary patents claiming paritaprevir, ombitasvir and dasabuvir are "are likely to prevent the launch of generic products where they are granted and enforceable." Generic versions of Viekira Pak and Viekirax "will have to note the expiry of the patents on the individual components and of any patents covering their use in combination."

Other Initiatives

This is not the first overview of the patent position on a drug product class. That was published back in 2003 by Médecins sans Frontières for HIV medicines, 't Hoen noted. The MPP, which works with governments, industry, and other stakeholders on licensing needed medicines and encouraging generic manufacture and the development of new formulations through patent pooling, now has a patent database that provides information on selected HIV medicines in low- and middle-income countries and allows users to search by country/region and by product to obtain information on key patents.

The WHO's UNITAID, which finances the MPP, has also carried out some patent status studies, including on medicines for TB, 't Hoen noted. And in April this year, the MPP and the TB Alliance signed a *memorandum of understanding* to collaborate on developing licensing strategies for future TB drug regimens developed by the TB alliance, which includes the sharing of drug patent

status and other data.

The MPP and the European generic and biosimilar drugs industry body, Medicines for Europe, declined to provide a comment for this article.

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