PATENT SITUATION OF KEY PRODUCTS FOR TREATMENT OF HEPATITIS C

PARITAPREVIR/OMBITASVIR/DASABUVIR

WORKING PAPER

Revised version

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World Health Organization

This report was prepared for the WHO Department of Essential Medicines and Health Products by Thomson Reuters and Pharmathen. It is available for free download: http://www.who.int/phi/en/. If you have questions or feedback, please write to phidepartment@who.int.

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INTRODUCTION

The World Health Organization's (WHO) 2016 *Guidelines for the screening, care and treatment of persons with hepatitis C infection* states that more than 110 million people are infected with the hepatitis C virus (HCV) worldwide. Of these individuals, approximately 700,000 die from their infection annually and another 80 million progress to chronic infection within their lifetime. An estimated one third of those individuals who become chronically infected develop liver cirrhosis or hepatocellular carcinoma. HCV infection is curable, but most infected individuals are unaware of their illness and thus do not seek timely treatment. Furthermore, treatment remains unavailable for many who have been diagnosed. Several medicines available to treat HCV, such as pegylated interferon and ribavirin involve long treatment courses of weekly injections and considerable side effects. With the development of new direct-acting antivirals, the treatment landscape is rapidly changing. These new antivirals are reaching cure rates of over 90% in persons with HCV infection across different genotypes, with fewer side effects and shorter treatment courses. Since WHO issued its first guidelines on HCV treatment in 2014, more treatments have been approved. WHO published its updated treatment guidelines in April 2016.[1]

Resolution WHA67.6, adopted by the Sixty-Seventh World Health Assembly, requested the Director-General "to work with national authorities, upon their request, to promote comprehensive, equitable access to prevention, diagnosis and treatment for viral hepatitis" and "to assist Member States to ensure equitable access to quality, effective, affordable and safe hepatitis B and HCV treatments and diagnostics, in particular in developing countries". Ensuring access to new treatments is a challenging task. In order for countries to identify ways of increasing access and affordability of new HCV medicines, they need clarity about patent status. To assess whether a medicine is patent protected in a certain country requires expert knowledge and access to specialized databases that are not easily available. The WHO Global strategy and plan of action on public health, innovation and intellectual property provides WHO with a mandate to support efforts to determine the patent status of health products (element 5.1c). Despite the possibility of filing patents under the World Intellectual Property Organization (WIPO) Patent Cooperation Treaty (PCT) in 148 jurisdictions, worldwide patents do not exist. Patents are granted individually under each jurisdiction, depending on the national patent law and the outcome of the examination process. National patents that relate to the same basic patent (i.e. the same invention) are called family members and together constitute a patent family. In the present study, patent families are based on the Derwent World Patent Index (DWPI).[2] In 2014, the WHO Secretariat mandated Thomson Reuters to carry out an analysis of the patent situation of

[1] Guidelines for the screening, care and treatment of persons with hepatitis C infection. Geneva: World Health Organization; 2016 (http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2016/en/, April 2016.)

[2] The Derwent World Patents Index (or DWPI) is a database containing patent applications. Each patent family is grouped around a basic patent, which is usually the first published example of the invention.

seven new hepatitis treatments.[3] The draft and updated reports were shared with the respective sponsor companies before publication. Due to the fast developing patent situation, in August 2015 WHO mandated another service provider, Pharmathen, to update and revise reports and the relevance of the different patents included in these reports.

International nonproprietary name	**Sponsor**
daclatasvir	Bristol-Myers Squibb Company
dasabuvir	AbbVie Inc.
ledipasvir	Gilead Sciences, Inc.
ombitasvir	AbbVie Inc.
paritaprevir	AbbVie Inc.
simeprevir	Janssen Pharmaceutical Companies of Johnson & Johnson
sofosbuvir	Gilead Sciences Inc.

OBJECTIVE

The objectives of the patent working papers are to:

1. identify the most relevant patents with respect to the medicines of interest
2. identify in which countries these patents have been filed and granted
3. identify secondary patents that might delay the entry of generic medicines

The patent working papers identify the most relevant patents for each medicine. The patents are categorized as primary and secondary patents. The patent publications on the base compound are considered “primary patents” and the patents on specific pharmaceutical formulations, methods of use, product derivatives, and processes are considered “secondary patents”. Secondary patents are generally easier to circumvent or “to invent around”, meaning that medicines can be formulated such that they do not infringe on the claims of the secondary patent For example, a patent on an aqueous form of a medicine would not prevent competitors from producing a tablet form, and a combination patent would not prevent competitors from producing the combined products separately. The report highlights those secondary patents that may delay generic entry.

[3] Initially, two additional candidate medicines were included in the project (faldaprevir and deleobuvir), but development of these products has been discontinued. Thus, the patent landscapes were not finalized.

The following are different types of patents:

Product patents claim the chemical molecule/the active pharmaceutical ingredient. Product patents are usually the strongest patents as the patent holder can use product claims to prevent others from making, selling, or importing the chemical product.

Product-by-process patents define the product by its process of preparation.

Process patents claim a (new) production process for an active pharmaceutical ingredient.

Formulation patents relate to the specific dosage form (e.g. coated tablet, soft gel capsule, syrup etc.).

Combination patents claim the combination of new or existing medicines.

Patents on product derivatives claim a specific form or derivative (e.g. a salt of an existing compound).

Patents containing Markush claims refer to a chemical structure with multiple alternatives in a format such as "chemical compound A wherein X^1 is selected from a group consisting of a, b and c".

This list is simplified and not exhaustive. Detailed explanations can be found in Philip Grubb, Peter Thomsen, *Patents for Chemicals, Pharmaceuticals, and Biotechnology*, 5th Edition Oxford 2010, as well as in the patenting guidelines of the respective national or regional patent offices.

Interpretation of patentability criteria varies, in particular with respect to the so-called secondary patents. Some jurisdictions are more restrictive to prevent a proliferation of secondary patents covering minor modifications of existing medicines. In those jurisdictions, for example, India and Argentina, many of the secondary patents may not be granted as they do not fulfil their specific requirements. Further information can be found in the draft *Guidelines for the examination of pharmaceutical patents: developing a public health perspective* which provides detailed information on the different forms of patents in the pharmaceutical sector (www.who.int/phi/publications/category/en/).

HOW TO USE THIS WORKING PAPER?

Each working paper identifies the relevant patents and provides data where these patents have been filed or granted. They allow countries to carry out a first assessment on whether a medicine is patent protected and to explore affordable treatment schemes. The data is also essential to allow the WHO to fulfil its mandate under Resolution WHA67.6, which requests the WHO to assist Member States in ensuring equitable access to quality, effective, affordable and safe HCV treatments. Assisting countries in accessing the new HCV treatments at an affordable price requires knowledge about the patent situation in the respective jurisdictions as this determines the various options countries have.

The working papers can also help other interested parties negotiate the transfer of technology and license agreements, develop research methods to improve the current drug or treatment modality, and facilitate the development of generics.

Although considered public domain material, patent information in many countries is difficult to retrieve, as reflected by the gaps in the Annex. N/A indicates that no information could be retrieved for the relevant patents in the databases that were used. This can either signify that the information in the databases is not up-to-date or complete, or that the patents were not filed in these jurisdictions. While the latter may often be the case, certainty can only be achieved by checking the information with the local patent office. This can be done by using the patent numbers provided in this report, as they allow retrieval of information through national patent offices and/or national patent registries. The following WIPO page provides links to all national online patent search tools to search national patent registries: http://www.wipo.int/branddb/portal/portal.jsp.

For international patent searches Patentscope and Espacenet can be used:

https://patentscope.wipo.int/search/en/search.jsf

http://worldwide.espacenet.com/

LIMITATIONS

While endeavours have been made to make the content of this study accessible to the non-expert, the highly technical nature of the subject matter and the singularities of the patent system require certain expertise to make full use of this study.

Every effort has been made to obtain comprehensive and accurate information, including on the legal status of the patents. However, in many countries, patent information is not readily available or updated on a regular basis. In addition, some patent applications may have been published only after the searches were conducted, and thus may not be included in this study. As this study endeavours to identify the most relevant patents, it does not include all patents and applications filed by the Sponsor and other entities that also relate to the different treatments.

It should also be noted that this study is not a freedom-to-operate analysis. The information provides useful guidance, but only reflects the situation at a particular point in time. Neither the WHO nor Thomson Reuters or Pharmathen accept any responsibility for the accuracy of data, nor guarantee that it is complete or up-to-date. **Users are advised, before taking any investment or other legally relevant decision, to consult a local patent expert to assess the patent situation in a given country.**

METHODOLOGY

The initial working papers outline relevant patents and patent applications in countries included as of March 2014. Relevant patents and patent applications were identified by searching patent and non-patent databases comprised of Thomson Innovation, Newport, Thomson Pharma, Questel, Scientific Technology Network (STN) and Cortellis. For Patent 1 daclatasvir, the original data was kindly complemented by the Sponsor Bristol-Myers Squibb. The update of the original study includes patents published up to June 2016. Patents included in the original report were reviewed for relevance. Those considered less relevant or irrelevant were removed and new patents were added.

The annex includes information directly retrieved or received from the following patent offices: ARIPO, Brazil, Chile, Egypt, GCC, Georgia, Jordan, Malaysia, Morocco, OAPI, Peru, Philippines, Thailand, Tunisia and Vietnam. Additional information was received by the Medicines Patent Pool and Oscar Lizarazo from the National University of Colombia.

Information submitted under Section 8 of the Indian Patents Act 1970

Section 8 of the Patents Act on Information and undertaking regarding foreign applications requires the applicant for a patent to file a statement setting out detailed particulars of any applications in countries outside India in respect of the same invention and to update this information in writing, from time to time. The Patent Rules 2003 (as of March 2015) concretize that this information shall be filed by the applicant for a patent through the Form 3 within six months from the date of filing the application.

The data found for each of the patents listed in the Annex was compared to the latest Form 3 as submitted to the Indian Patent Office for the corresponding Indian family member. Any missing information was included in the Annex. For territories where no corresponding filing was identified in the data search and for which no corresponding filing was listed in Form 3 the information contained in the Annex was changed from “N/A” to “Not filed” with a reference to Form 3 as the source of information, provided that the respective Form 3 was dated at least 3 years after the International Patent Cooperation Treaty filing date.

The Form 3 for each patent filing in India can be found by searching on the Indian patent office website for the Indian patent and afterwards select view documents: http://ipindiaonline.gov.in/patentsearch/search/index.aspx

Since the Form 3 lists for paritaprevir, ombitasvir and dasabuvir have not been updated regularly, only two Form 3 lists where used in this report to add three patents to the annex.

The following Form 3 lists where used to check and complete data in the annex:

Patent 17, Indian Patent number 276/DELNP/2013 Form 3 dated 9 July 2013.

Patent 18, Indian Patent number 638/DELNP/2013 Form 3 dated 19 July 2013.

Where available, the application submitted under the WIPO PCT is used as a primary source, both because a) it is generally the favoured priority application for the pharmaceutical industry, and b) the WIPO International Search Report (ISR) includes

examiner references that are coded for relevance and for which initial rejections (an indicator of possible novelty issues) can be identified. Technical experts from the service providers analysed the claims. Where available, the outcome of the WIPO ISR on novelty and inventive step is described. It should be noted that quotes from the ISR are only examples and do not preclude objections or outcomes under national jurisdictions.

The expected time of expiration for all the patents was calculated and can be found in the Annex.

US ORANGE BOOK

The updated Annex indicates which of the listed patents are contained in the US Orange Book of the US Federal Drug Administration (FDA). The US Orange Book lists the patents as submitted by the holder of the authorization with respect to new medicines authorized by the FDA for the US market. Under FDA rules, the holder of the authorization has to notify certain patents, including formulation/composition patents and use patents for a particular approved indication or method of product use. Process patents, for example, do not need to be notified (FDA Orange Book, 36th Edition 2016).

GEOGRAPHIC SCOPE

Family members of the Sponsor patent collection have been searched for in the following jurisdictions. It is beyond the scope of this study to include patent information of all WHO Member States, thus selection was made taking into account disease burden, local manufacturing capacities and regional representation:

Argentina (AR), African Regional Intellectual Property Organization (AP), Australia (AU), Brazil (BR), Canada (CA), Chile (CL), China (CN), China, Hong Kong SAR (HK), Colombia (CO), Costa Rica (CR), Ecuador (EC), Egypt (EG), European Patent Office (EPO), Ethiopia (ET), Eurasian Patent Office (EAPO), Georgia (GE), India (IN), Indonesia (ID), Iran (Islamic Republic of) (IR), Israel, (IL), Japan, Jordan (JO), Malaysia (MY), Mexico (MX), Morocco (MA), New Zealand (NZ), Nigeria (NG), African Intellectual Property Organization (OA), Pakistan (PK), Patent Office of the Cooperation Council for the Arab States of the Gulf (GCC), Peru (PE), Philippines (PH), Republic of Korea (KR), Russian Federation (RU), Singapore (SG), South Africa (ZA), Thailand (TH), Tunisia (TN), Ukraine (UA), the United States of America (US), Uruguay (UY), and Vietnam (VN).

FURTHER RESOURCES

The WHO publication *How to conduct patent searches for medicines: a step-by-step guide* provides guidance on how to identify the patent status of medicines.[4] The draft *Guidelines for the examination of pharmaceutical patents: developing a public health perspective* provides detailed information on the different forms of patents in the pharmaceutical sector.[5] Material on the relationship between public health and intellectual property can be found in the document *Promoting Access to Medical Technologies and Innovation. Intersections between public health, intellectual property and trade*.[6] These publications as well as other relevant publications on issues related to public health and intellectual property can be found here: www.who.int/phi/publications/category/en/

More information on HCV and the recommended treatments can be found here: www.who.int/topics/hepatitis/en/

PATENT OPPOSITIONS AND LITIGATION

There are an increasing number of patent oppositions and litigation cases with respect to the new HCV drugs, sofosbuvir in particular. While the reports highlight some opposition and litigation cases, due to the high number of cases, it is beyond the scope of these reports to cover all these cases. Information on current opposition procedures can be found in relevant patent registers (see above) as well as on:

http://www.patentoppositions.org/

http://www.i-mak.org/

[4] How to Conduct Patent Searches for Medicines: A Step-by-Step Guide. Delhi: World Health Organization; 2010 (http://www.wpro.who.int/publications/PUB_9789290223757/en/, May 2016.)
[5] Guidelines for the examination of pharmaceutical patents: developing a public health perspective. Geneva: World Health Organization; 2006 (http://apps.who.int/medicinedocs/documents/s21419en/s21419en.pdf, May 2016.)
[6] Promoting Access to Medical Technologies and Innovation. Intersections between public health, intellectual property and trade. Geneva: World Health Organization, World Trade Organization, World Intellectual Property Organization; 2013 (http://www.who.int/phi/promoting_access_medical_innovation/en/, May 2016.)

Paritaprevir, Ombitasvir and Dasabuvir

AbbVie Inc., hereby referred to as the Sponsor[7], has developed an interferon-free regimen containing three direct acting antiviral agents (DAAs) with distinct mechanisms of action and non-overlapping resistance profiles for the treatment of chronic HCV infection:

- paritaprevir (ABT-450)
- ombitasvir (ABT-267)
- dasabuvir (ABT-333)

Paritaprevir is dosed with ritonavir (r), a potent CYP3A4 inhibitor administered at a low dose to improve the pharmacokinetics of paritaprevir. The combination of paritaprevir and ritonavir is represented as paritaprevir/r. This report covers the patent situation of all three products as they are used in combination to treat HCV.

In Europe, the treatment is marketed under the trade name Viekirax. It is a combination of 12.5 mg of ombitasvir, 75 mg of paritaprevir and 50 mg of ritonavir administered in a single film coated tablet. Per protocol, the treatment is to be given in combination with dasabuvir, ribavirin or both, depending on HCV genotype. Dasabuvir is marketed under the name Exviera in Europe and is only approved for use in combination with Viekirax.

In the United States, the treatment is marketed as a special pack under the tradename Viekira Pak. Viekira Pak contains four tablets packaged together in a wallet (two of each tablet). The first tablet pair contains the fixed-dose combination of ombitasvir, paritaprevir and ritonavir. The second tablet pair consists of 250mg of dasabuvir each Dasabuvir is not sold separately in the United States. Depending on the genotype, ribavirin also may be required. The fixed-dose combination of ombitasvir, paritaprevir and ritonavir bears the tradename Technivie.

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 updated treatment guideline of people infected with HCV from WHO, published in April 2016, recommends the use of paritaprevir, ombitasvir and dasabuvir as an alternative treatment option as these DAAs require a longer treatment course and have considerable side effects.

[7] Abbott separated its business in 2013 into two companies Abbott and AbbVie Inc., the latter taking over the area of hepatitis. Patents were filed by Abbott Laboratories (assigned to AbbVie Inc.) or by AbbVie Inc., and therefore remain in the name of the Sponsor entity AbbVie Inc.

PARITAPREVIR

Paritaprevir is a serine protease inhibitor, specifically targeting the activity of HCV NS3 protease. Consequently, the composition interferes with the HCV life cycle and therefore, may be used as an antiviral agent if boosted with ritonavir, a pharmacokinetic enhancer of paritaprevir.

Paritaprevir was first developed by Enanta Pharmaceuticals, under a 2006 collaboration agreement between Enanta and AbbVie Inc. The latter is responsible for the development, manufacture and commercialization of paritaprevir and funds all associated costs.

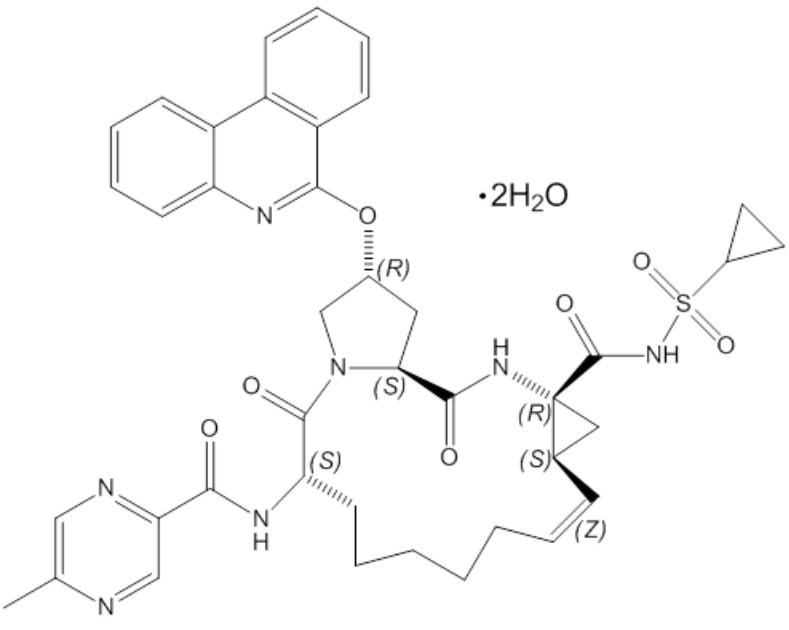
CHEMICAL NAME

(2R, 6S, 12Z, 13aS, 14aR, 16aS)-N-(cyclopropylsulfonyl)-6-{[(5-methylpyrazin-2-yl)carbonyl] amino}-5,16-dioxo-2-(phenanthridin-6-yloxy)-1,2,3,6,7,8,9,10,11,13a,14,15,16,16a-tetradeca hydrocyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a(5H)-carboxamide dihydrate

MOLECULAR FORMULA

$C_{40}H_{43}N_7O_7S \cdot 2H_2O$

MOLECULAR STRUCTURE



OMBITASVIR

Ombitasvir is an HCV NS5A protein inhibitor developed by AbbVie Inc. This drug inhibits the HCV non-structural protein 5A and is used for HCV treatment.

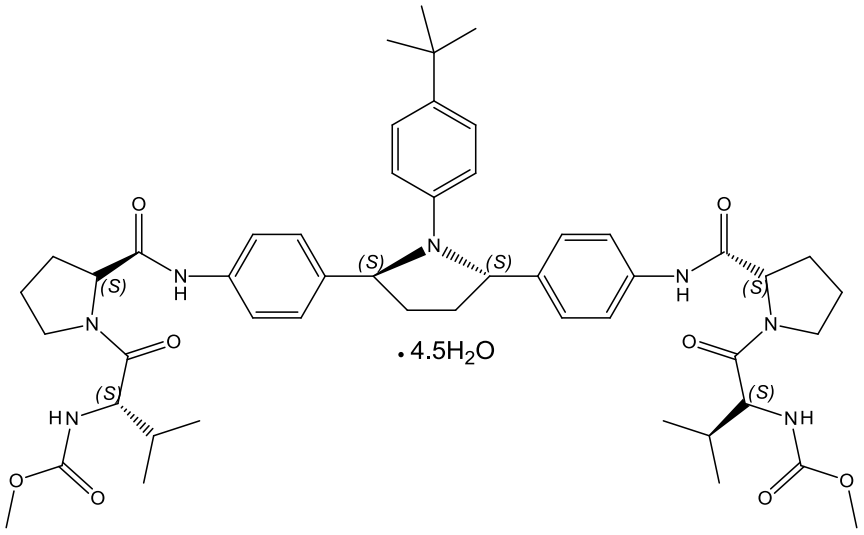
CHEMICAL NAMES

Dimethyl ([2S, 5S)-1-(4-tert-butylphenyl)pyrrolidone-2, 5-diyl]bis{benzene-4, 1-diylcarbamoyl (2S)pyrrolidine-2, 1-diyl{(2S)-3-methyl-1-oxobutane-1, 2-diyl]}) biscarbamate hydrate

MOLECULAR FORMULA

$C_{50}H_{67}N_7O_8 \cdot 4.5H_2O$

MOLECULAR STRUCTURE



DASABUVIR

Dasabuvir is a viral polymerase inhibitor developed by AbbVie Inc. This drug inhibits the non-nucleoside HCV NS5B polymerase and is used for HCV treatment.

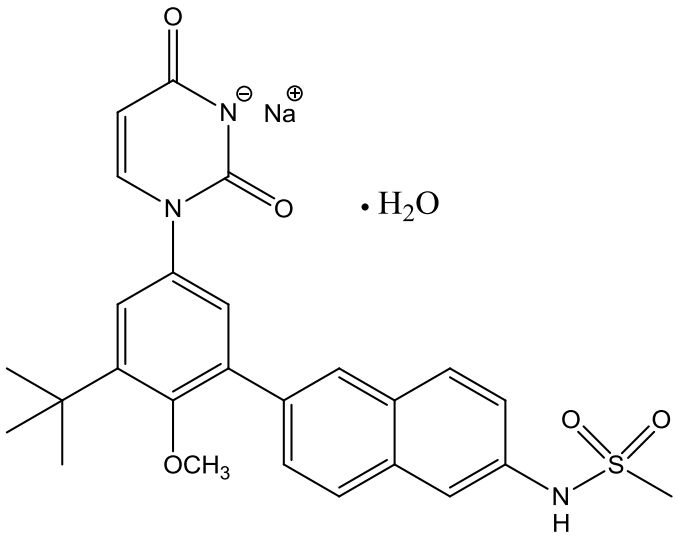
CHEMICAL NAME

Sodium *N*-(6-{3-*tert*-butyl-5-[2, 4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-2-methoxyphenyl} naphthalen-2-yl)methanesulfonamide hydrate

MOLECULAR FORMULA

$C_{26}H_{26}N_3O_5SNa \cdot H_2O$

MOLECULAR STRUCTURE



Though part of this combination treatment, ritonavir has no direct therapeutic value in treating HCV. It is used at a “low dose” to improve the pharmacokinetics of paritaprevir.

SUMMARY

The search revealed 20 patents by the Sponsor filed with respect to paritaprevir, ombitasvir, dasabuvir and any combination of the three.

Patent 1 (WO2010030359) is a primary patent, claiming the compound of paritaprevir, a method for its production and its pharmaceutical composition.

Patent 2 (WO2010144646) is a primary patent, claiming the compound of ombitasvir through a Markush claim, along with various substituents.

Patent 3 (WO2009039134 or WO2009039127[8]) is a primary patent, claiming the compound of dasabuvir through a Markush claim, along with various substituents.

These three patents are likely to prevent the launch of generic products where they are granted and enforceable. Generic products of VIEKIRA PAK (ombitasvir/paritaprevir/ritonavir, dasabuvir) and VIEKIRAX (ombitasvir/paritaprevir/ritonavir) will have to note the expiry of the patents on the individual components and of any patents covering their use in combination.

Patent 4 (WO2011112558) relates to solid compositions comprising amorphous paritaprevir, a hydrophilic polymer and a surfactant that reduces the surface tension of water. It is a formulation patent, claiming the pharmaceutical dosage form (pharmaceutical composition) used in the Sponsor's product VIEKIRAX.

Patent 5 (WO2011156578) is a formulation patent, claiming the pharmaceutical dosage form (pharmaceutical composition) used in the Sponsor's product VIEKIRAX. The claimed formulation comprises ombitasvir and a hydrophilic polymer in the form of a solid dispersion for HCV treatment.

According to the public evaluation reports at the European Medicines Agency, the VIEKIRAX product is an amorphous solid dispersion form of the active ingredients. It is stated that this form improves the low solubility and bioavailability of paritaprevir and ombitasvir. Patents 4 and 5 may constrain the release of generic products if alternative technologies are not found to reproduce the required level of equivalent bioavailability in a generic version of VIEKIRAX.

Patent 6 (WO2013059630) relates to interferon-free therapies for the treatment of HCV.

Patent 7 (WO2013059638) relates to features of interferon- and ribavirin-free therapies for the treatment of HCV.

[8] WO2009039134 and WO2009039127 were filed on the same day. In certain countries, one application serves exclusively as the relevant international patent application over the other. In other countries, both applications have entered into the national phase and are pending.

Patents 6 and 7 are relevant to combinations with and of other DAAs such as daclatasvir, ledipasvir, simeprevir, sofosbuvir. These patents are thus relevant for combination treatments of all these DAAs. These patents are in litigation.

Patent 8 (WO2013040568A1) relates to a combination comprising paritaprevir, ritonavir and another anti-HCV agent with or without ribavirin.

Patent 9 (WO2013101552) claims ombitasvir for use in a combination therapy with another anti-HCV agent in which the treatment is interferon-free.

Patent 10 (WO2014004674) relates to a combination of an HCV protease inhibitor with ritonavir to treat HCV infection.

Patent 11 (WO2014063101) claims a composition comprising dasabuvir and at least one bioavailability enhancing agent.

Patent 12 (WO2014011840) relates to crystalline polymorphs of paritaprevir and identifies ten different unique solid forms of paritaprevir.

Patent 13 (WO2015002952) claims interferon-free therapies for treating HCV genotype 1b, 2, 3 or 4, and is centred on paritaprevir and ombitasvir administration. Preferably the therapies do not include administration of ribavirin.

Patent 14 (WO2015071488) relates to a solid composition comprising paritaprevir, ombitasvir and ritonavir which are co-formulated in an amorphous solid dispersion. This patent, which claims the amorphous form and solid dispersion of paritaprevir, represents a significant barrier for companies that wish to develop generic versions of paritaprevir.

Patent 15 (WO2015084953) relates to crystalline polymorphs of paritaprevir. It claims alternative forms of solid crystalline paritaprevir not claimed in Patent 12.

Patent 16 (WO2015103490) relates to a solid dosage form comprising paritaprevir, ombitasvir, ritonavir and dasabuvir for the treatment of HCV infection. The application represents an exemplary formulation, disclosing a bilayer tablet. This product has not been approved or launched, but would be relevant should VIEKIRAX and EXVIERA be marketed as a one tablet combination product. This patent is listed in the report for future reference should the proposed combined product be launched.

Patents 17 to 19 are process patents related to dasabuvir.

Patent 20 is a process patent related to paritaprevir.

PATENT 1: Paritaprevir

This patent is listed in the US Orange Book for VIEKIRA PAK and TECHNIVIE with patent numbers US8420596 and US8642538.

Patent application WO2010030359A2 is the primary and constraining patent, claiming the compound of paritaprevir, a method for the production of paritaprevir as well as its pharmaceutical composition. Where granted, this patent serves as the blocking patent preventing competitors from making, selling and using products containing paritaprevir.

PATENT 2: Ombitasvir

This patent is listed in the US Orange Book for VIEKIRA PAK and TECHNIVIE with patent numbers US8691938, US9006387.

Patent application WO2010144646A2 is a primary patent disclosing the base compound of ombitasvir. The patent claims a general structural formula or Markush structure of the basic compound as well as its various substituents. This patent, if granted, serves as a blocking patent preventing competitors from making the product.

PATENT 3: Dasabuvir

Patent WO2009039134 is listed in the US Orange Book for VIEKIRA PAK and TECHNIVIE with patent numbers US8188104, US8501238 and US9139536.

Both patent applications WO2009039134A1 and WO2009039127A1[9] cover the base compound of dasabuvir, claiming a general structural formula of pyrimidine compounds and salts of dasabuvir for use in the inhibition of ribonucleic acid viral replication and therefore applicable to HCV treatment. This patent, if granted, serves as a blocking patent preventing competitors from making the product. The claims are very broad, covering a Markush structure of antiviral agents.

PATENT 4: Paritaprevir

Patent application WO2011112558A1 relates to solid composition comprising paritaprevir in amorphous form, a hydrophilic polymer and a surfactant that reduces the surface tension of waterfor use in HCV treatment. Combination of ritonavir with the above composition is also disclosed.

Per the European Medicines Agency public evaluation reports, VIEKIRAX uses an amorphous solid dispersion of the active ingredients to improve the low solubility and bioavailability of paritaprevir and ombitasvir. This patent can block the launch of generic products if alternative technologies are not developed to reproduce the required level of equivalent bioavailability found in VIEKIRAX in a generic version. The patent also claims a process for preparing a composition.

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[9] WO2009039134 and WO2009039127 were filed on the same day. In certain countries, one application serves exclusively as the relevant international patent application over the other. In other countries, both applications have entered into the national phase and are pending.

PATENT 5: Ombitasvir

This patent is listed in the US Orange Book for VIEKIRA PAK and TECHNIVIE with patent number US8686026.

Patent application WO2011156578A1 claims a pharmaceutical formulation of ombitasvir, including a solid composition of one of four substituted pyrrolidine derivatives in an amorphous form for the treatment of HCV infection.

Per the European Medicines Agency public evaluation reports, VIEKIRAX uses an amorphous solid dispersion of the active ingredients to improve the low solubility and bioavailability of paritaprevir and ombitasvir. This patent can constrain the launch of generic products if alternative technologies are not found to reproduce the required level of equivalent bioavailability found in VIEKIRAX. The patent also claims a process for preparing the composition.

PATENT 6: Combination

This patent is listed in the US Orange Book for VIEKIRA PAK with patent numbers US8466159 and US8680106.

Patent application WO2013059630A1 claims the use of a combination of ribavirin and at least two DAAs for an interferon-free treatment for HCV in which treatment lasts 8-12 weeks. The combination of paritaprevir and ombitasvir is specifically claimed in dependent claims. Preferably, the therapies involve interferon- and ribavirin-free regimens of at least two DAAs for HCV-infected individual. Where granted and enforceable, this patent could prevent the development of generic versions of these products.

PATENT 7: Combination

This patent is listed in the US Orange Book for VIEKIRA PAK with patent numbers US8492386, US8685984.

The patent application WO2013059638A1 is a formulation patent, claiming an interferon- and ribavirin-free combination of at least two DAAs alone or in combination with ritonavir. The DAAs included are selected from paritaprevir, dasabuvir, daclatasvir, sofosbuvir, simeprevir, ledipasvir, asunaprevir and BMS-986094. VIEKIRA PAK and VIEKIRAX are approved for use without ribavirin and interferon in genotype 1b. Where granted and enforceable, this patent may prevent the marketing of generic versions of these products, including a combination of sofosbuvir, daclatasvir or others.

Note: Patents 6 and Patent 7 inter alia claim the use of combinations of unnamed direct-acting antiviral agents for treating HCV, where treatment is interferon- or ribavirin-free and lasts 8-12 weeks. These patents are thus relevant to combinations of other DAAs as well as such as daclatasvir, ledipasvir, simeprevir, sofosbuvir, as they claim the use of combinations of all those DAAs. These patents are in litigation.

Litigation / Opposition on Patents 6 and 7

Gilead Sciences, Inc. filed a patent infringement lawsuit against Abbott Laboratories, Inc. and AbbVie, Inc. (collectively “Abbott”) on 18 December 2013 in the United States District Court for the District of Delaware (Case no 1:13-cv-02034). The Gilead and Abbott patents involved are US8088368B2, US8492386B2, US8466159B2, US8273341B2, US8575118B2, US7964580B2, US8334270B2, and US8580765B2, with the last three relating to Gilead Sciences Patent 2 in the sofosbuvir report.

The original complaint is sealed. According to a redacted complaint, the defendants falsely and knowingly represented themselves to the USPTO as the inventors of the HCV treatment methods that were, in fact, invented by the plaintiffs. The plaintiffs requested the court to issue a declaratory judgment that claims 13–16 of the ’159 and ‘386 patents are invalid. The plaintiffs also ask the court to issue a declaratory judgment that the ’159 and ‘386 patents are unenforceable, alleging misconduct on the part of the defendant. In a Joint Status Report dated 21 January 2015, the plaintiff seeks restitution and damages for the defendants’ conduct as described above, and a declaration as to the invalidity, non-infringement and unenforceability of a number of patents.

Plaintiff Abbott Laboratories, Inc. and AbbVie, Inc. (collectively “Abbott”) filed two patent infringement lawsuits against Gilead Sciences on 18 February 2014 and 25 March 2014 in the United States District Court for the District of Delaware (Case no 1:14-cv-00209 and Case no 1:14-cv-00379).

PATENT 8: Paritaprevir

Patent application WO2013040568A1 claims interferon-free combination treatments comprising paritaprevir, ritonavir and another anti-HCV agent. The latter can be an HCV polymerase inhibitor, an HCV NS5A inhibitor, an HCV entry inhibitor, a CD81 inhibitor or an internal ribosome entry site inhibitor. The application claims this triple combination with or without ribavirin. The treatment does not claim a fixed-dose combination, but rather a concurrent or sequential administration of the compounds.

PATENT 9: Ombitasvir

Patent application WO2013101552A1 claims combinations of ombitasvir (a pyrrolidine dicarbamate derivative) and one other anti-HCV agent for use in interferon-free treatment of HCV infection. Similar to Patent 8, the combination treatments can be administered with or without ribavirin. Possible anti-HCV agents include HCV polymerase inhibitors, HCV protease inhibitors, HCV entry inhibitors, cyclophilin inhibitors, CD81 inhibitors, or internal ribosome entry site inhibitors (but not NS5A inhibitors, as ombitasvir is an NS5A inhibitor). Unlike Patent 8, the combination does not include ritonavir.

PATENT 10: Ritonavir

Patent application WO2014004674A1 relates to the combination of a HCV protease inhibitor (preferably paritaprevir or less preferably danoprevir) with ritonavir for treating HCV

infection. The patent focuses on ritonavir's activity as a pharmacokinetic enhancer. Ritonavir inhibits the enzyme CYP3A4 and thus boosts the effect of molecules metabolized by this enzyme – this includes many anti-HCV agents. In the past, the use of ritonavir required monitoring of patient cholesterol and tri-glyceride levels. This is not the case when used in combination with HCV protease inhibitors. In fact, VIEKIRA PAK and VIEKIRAX do not recommend cholesterol or tri-glyceride monitoring on their labels, so this patent will be relevant where granted.

According to the WIPO ISR, this patent lacks unity of invention. It is considered that while the subject-matter of the dependent claims are considered novel, they do not contribute any further technical features to allow for the recognition of inventiveness at present.

PATENT 11: Dasabuvir

Patent application WO2014063101A1 relates to a pharmaceutical composition comprising pyrimidinedione derivative compounds and at least one bioavailability enhancing agent. Dasabuvir is specifically mentioned in the dependent claim.

PATENT 12: Paritaprevir

Patent application WO2014011840A1 relates to crystalline polymorphs of paritaprevir.

It is reported in the public assessment report for paritaprevir by the European Medicines Agency that the drug substance is consistently manufactured in crystalline form and is converted to an amorphous form before extruded into a solid dispersion to improve the dissolution and solubility of the final product.

PATENT 13: Paritaprevir /r + ombitasvir

Patent application WO2015002952A1 claims interferon-free therapies for treating HCV genotype 1b, 2, 3 or 4, involving administration of paritaprevir and ombitasvir, preferably without ribavirin. To improve pharmacokinetics, the combination should be co-administered with ritonavir or another CYP3A4 inhibitor. The patent also gives concrete dosage examples for each of the compounds and suggests a solid co-dosage form.

Currently, administration of ombitasvir without ribavirin is only approved for HCV genotype 1b. If claims are granted covering ombitasvir in a ribavirin-free therapy for HCV genotype 1b, this patent may be a barrier in the launch of a generic version.

PATENT 14: Paritaprevir /r + ombitasvir

Patent 13, application WO2015071488A1, describes a solid fixed-dose composition comprising paritaprevir, ombitasvir and ritonavir, but proposes an improved formulation. As both paritaprevir and ombitasvir are poorly soluble, the improved method proposes co-formulation of the compounds in a solid dispersion of their amorphous forms to increase solubility.

Where granted and enforceable, this patent represents a significant barrier for companies that wish to develop generic versions of VIEKIRA PAK or VIEKIRAX.

PATENT 15: Paritaprevir

Patent application WO2015084953A1 relates to crystalline polymorphs of paritaprevir, which are alternative forms of solid crystalline paritaprevir not claimed in Patent 12.

PATENT 16: Paritaprevir /r + Ombitasvir + Dasabuvir

Patent application WO2015103490A1 relates to a dosage form of a combination of paritaprevir, ombitasvir, dasabuvir and ritonavir for HCV treatment. The application represents an exemplary formulation, disclosing a bilayer tablet. Currently the products are not sold as combination products, but as tablets co-packed as individual tablets. Therefore, this patent is not relevant to the development of generic products of VIEKIRA PAK. The patent would be relevant for the marketing of a combination of VIEKIRAX and EXVIERA as one product. This patent is listed in the report for future reference should the proposed combined product be launched.

PATENT 17: Dasabuvir

Patent application WO2012009698A1 is a product by process patent referencing dasabuvir. The application covers phosphine ligands for use in catalytic reactions. The application also claims a process for the preparation of dasabuvir or its isomers or homologs, for use in HCV treatment. The process and compound claims are broad in nature.

PATENT 18: Dasabuvir

This patent application WO2012009699A2 is a process patent, claiming a process for dasabuvir inhibition of HCV. The application also claims intermediates useful in preparing agents to treat HCV infections. The process claims are moderately narrow in nature, claiming a process directed toward the formation of specific compounds.

PATENT 19: Dasabuvir

This patent application WO2014031791A1 is a process patent, claiming processes for preparing pyrimidine derivatives, particularly dasabuvir and its salts. The application also claims intermediates useful in preparing agents to treat HCV infections.

PATENT 20: Paritaprevir

Patent application WO2013106631 is a process patent related to paritaprevir. Intermediate compounds used in the process are also claimed.

ANNEX – PARITAPREVIR/OMBITASVIR/DASABUVIR PATENT SITUATION

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
Subject Matter	Patent application WO2010030359 claims the compound of paritaprevir.	Patent application WO2010144646 claims a general structural formula of the compound of ombitasvir as well as its various substituents.	Patent application WO2009039134 or WO2009039127 covers the base compound of dasabuvir.	Patent application WO2011112558 covers a solid composition comprising amorphous paritaprevir, hydrophilic polymer and a surfactant.	Patent application WO2011156578 claims a pharmaceutical formulation of ombitasvir and/or paritaprevir.	Patent application WO2013059630 claims interferon-free therapy containing at least two direct acting antiviral agents.	Patent application WO2013059638 claims interferon- and ribavirin-free therapy containing at least two direct acting antiviral agents.
Applicant	Enanta / Abbott	Abbott	AbbVie Inc.	Abbott	Abbott	Abbvie	Abbvie
Int'l Patent Publication Number	WO2010030359A2	WO2010144646A2	WO2009039134A1 WO2009039127A1	WO2011112558A2	WO2011156578A1	WO2013059630A1	WO2013059638A1
Priority Number	US20080191725P US20090209689P	US2009186291P	US2007972881P US20070972877P US20080096791P	US20100339964P	US2010813301A	US201161550352P US201161562181P US201261587225P US201261600276P US201261619870P US201261656251P US201261711830P	US201161550360P US201161562176P US201261587197P US201261600468P US201261619883P US201261656253P US201261711793P
Expected expiry[1]	10 Sept 2029	9 Jun 2030	16 Sep 2028	08 Mar 2031	8 Jun 2031	19 Oct 2032	19 Oct 2032
PATENT STATUS							

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
ARIPO (AP)[2]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Argentina (AR)	Status: N/A AR073568A1 Status: N/A AR086181A2	Pending AR77060A1 Status: N/A AR0833398A1	Granted[7] AR70027A1	Status: N/A AR081736A1	Status: N/A AR083240A1	Status: N/A AR088463A1	Status: N/A AR088408A1
Australia (AU)	Granted AU2009292182B2 Granted AU2012201327B2 Pending AU2013205039A1 Pending AU2013205040A1	Granted AU2010258769B2 Granted AU2012203474B2 Pending AU2012247053A1	Granted:[7] AU2008302448B2 Lapsed[7] AU2013202002A1 Pending[7] AU2014280939A1	Granted AU2011224558B2	Granted AU2011264823B2	Granted AU2013201406B2 Granted AU2013201758B2 Pending AU2015201020A1 Granted AU2015100275 Granted AU2015100283 Granted AU2015100285 Granted AU2015100972 Granted AU2015100973	Granted AU2013201532B2 Granted AU2013201585B2 Pending AU2015200715A1 Granted AU2015100277 Granted AU2015100278 Granted AU2015100279 Granted AU2015100968 Granted AU2015100969 Granted AU2015100970 Granted AU2015100971

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
Brazil (BR)	Status: N/A BRPI0918724A2 Pending BR122012005261A2	N/A	N/A	N/A	Pending BR2120120315000	N/A	N/A
Canada (CA)	Pending CA2736895A	Granted CA2737601C	Granted CA2699986C	Granted CA2792601C	Pending CA2802180A1	Granted CA2811203C	Granted CA2811250C
Chile (CL)	N/A	Status: N/A CL20110689	Status: N/A[7] CL2008/2794	Status: N/A CL2012002500	Status: N/A CL2012003470	Pending CL2014000777	Pending CL2014000778
China (CN)	Granted CN101775017B Granted CN102641271B Pending CN103896950A	Granted CN102333772B Granted CN103172620B	Granted CN101842360B Pending CN102746240A Pending CN104628654A Pending CN104628655A	Granted CN103118681B Pending CN104771364A	Granted CN103209686B	Pending CN103826627	Pending CN104023726A Pending CN104436197A
China, Hong Kong SAR (HK)	Granted HK1159515 Granted HK1170936 Granted HK1171184	Pending HK1152620A0 Pending HK1161245A0 Pending HK1170739A0	Pending HK1148273A0 Pending HK1156033A0 Pending HK1177457A0	Pending HK1178058	Pending HK1184068	Pending HK1200015 Pending HK1199816 Pending HK1182316	Pending HK1182317 Pending HK1200022
Colombia (CO)	Granted CO6341565	Granted CO6440538A2	Status: N/A[7] CO6260076A2	Refused CO6640208A	Granted CO6660490	N/A	N/A
Costa Rica (CR)	Status: N/A CR20140180	N/A	Status: N/A[7] CR11316A	N/A	Status: N/A CR20120650A	N/A	N/A

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
Ecuador (EC)	Status: N/A ECSP11010879A Status: N/A ECSP12011947A	Status: N/A EC2011SP010937A	Status: N/A[7] SP-2010/10038	Status: N/A ECSP12012148A	Status: N/A ECSP201312382	N/A	N/A
Egypt (EG)	N/A	Status: N/A PCT/NA2011/503	Status: N/A[7] EG2010030435	N/A	Status: N/A EG2039/2012	N/A	N/A
Ethiopia (ET)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
EAPO (EA)[3]	Granted EA020582B1 Pending EA201200390A	Granted EA020031B Pending EA201300495A1	N/A	Granted EA021570B Status: N/A EA201290892	Status: N/A EA201291394A1	Pending EA201490837A	Pending EA201490836A
EPO (EP)[4]	Granted EP2340029B1 Granted EP2468285B1 Granted EP2468286B1 Granted EP2468287B1 Pending EP2805726A1	Pending EP2337781A2 Granted EP2368890B1 Pending EP2455376A1 Pending EP2628481A1	Granted EP2203431B1 Pending EP2368882A1 Pending EP2639226A1	Pending EP2544689A2	Granted EP2579854B1	Pending EP2583677A2	Pending EP2583680A2
GCC[5]	N/A	Status: N/A GC2010/16058	Status: N/A[7] GC2008/11746	N/A	Status: N/A GC2011/18566	N/A	N/A
Georgia (GE)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
India (IN)	Pending 7222/DELNP/2009	Pending 1475/KOLNP/2011 Pending 1423/KOLNP/2013	Pending 2627/DELNP/2010 Pending[7] 2632/DELNP/2010	Pending 2861/KOLNP/2012	Pending 11220/DELNP/2012	N/A	N/A
Indonesia (ID)	N/A	N/A	Status: N/A[7] IDW00201000841	N/A	Status: N/A ID201300071	N/A	N/A
Iran (Islamic Republic of) (IR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Israel (IL)	Granted IL211408 Pending IL218441 Pending IL234969	Granted: IL211792D0 Granted IL229248D0	Pending[7] IL204547	Pending IL221833	Pending IL223535	Pending IL230625 Abandoned IL230747	Pending IL230862D0
Japan (JP)	Granted JP5259537 Granted JP5534533 Pending JP2013163680 Pending JP2013227314	Granted JP5530514B	Granted JP5734655B Pending JP2013056886A	Granted JP5717768B2 Pending JP2015145387A	Granted: JP5814356B2	Granted JP5677645	Granted JP5677646

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
Jordan (JO)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Malaysia (MY)	Pending MYPI2011001033	Pending MYPI2011001412	Pending[7] MYPI2010001141	Pending MYPI2012700621	Pending MYPI2012701110	Pending MYPI2014700348	Pending MYPI2014700337
Mexico (MX)	Granted MX2011002486	Status: N/A MX2011005673A	Status: N/A MX2010002902A	Pending MX2012010478A	Granted MX2012014384	Pending MX2014004727A	Pending MX2014004729A
Morocco (MA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
New Zealand (NZ)	Granted NZ592170	Granted NZ591973A Granted NZ605773A	Granted[7] NZ584720A	Granted NZ602288	Granted NZ605440	Pending NZ609052 Pending NZ712227	Pending NZ625539 Pending NZ712223
Nigeria (NG)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
OAPI[6]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pakistan (PK)	N/A	N/A	Status: N/A[7] PK1098/2008	N/A	Status: N/A PK20110424	N/A	N/A
Peru (PE)	Granted PE07042011 Status: N/A PE13122012 Status: N/A PE09612014A1	Status: N/A PE20110679A1	Status: N/A[7] PE20130209A1 Status: N/A[7] PE20090705A1	Status: N/A PE01982013A	Status: N/A PE10362013A1	N/A	N/A

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
Philippines (PH)	N/A	Granted PH12011500637 Pending PH12015500289	Pending[7] PH12010500575 Pending[7] PH12013500365	Pending PH12012501784	Granted PH12012502442	Granted PH12014500832 Pending PH12014502848	Granted PH12014500833 Pending PH12014502847
Republic of Korea (KR)	Granted KR101379365B Granted KR101487726B1 Pending KR20140056195A	Pending KR2012117620A	Granted KR101552474 Pending KR20157010052	Granted KR20130048210	Granted KR101481395B Pending KR20150008151A	N/A	N/A
Russian Federation (RU)	N/A	N/A	Granted RU2539570C2 Pending[7] RU2010114828A	N/A	N/A	N/A	N/A
Singapore (SG)	Pending SG168922 Granted SG179414	Pending SG171708A1	Granted SG159964	Granted SG183985	Granted SG186251	Pending SG2014011647	Pending: SG2014011670
South Africa (ZA)	Granted ZA201200950 Pending ZA201101558	Granted ZA201102425A Granted ZA201203502A Granted ZA201300112A	Granted ZA201002689A	Granted ZA201207093	Granted ZA201300112	Pending ZA201400776 Pending ZA201507078 Pending ZA2015/07080	Pending ZA201400777 Pending ZA201406351 Pending ZA201406352
Thailand (TH)	N/A	N/A	Status: N/A[7] TH801004747	Status: N/A TH134236	Status: N/A TH1201006418	N/A	N/A

	Patent 1	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7
Tunisia (TN)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ukraine (UA)	Granted UA103054	Granted UA103052	Status: N/A UA201004147	Status: N/A UA201211694	Granted UA105434	Status: N/A UA201405390	Status: N/A UA201405392
The United States (US)	Granted US8420596B2 Granted US8642538B2 Pending US2014148573A1	Pending US20100317568A1 Pending US20110092415A1 Pending US20110207699A1	Granted US8188104B2 Granted US8501238B2	Pending US2011312973A	Granted US8686026B2 Granted US8716454B2 Abandoned US2014171481A	Pending US20130102557A1 Granted US8680106B2 Granted US8466159B2	Granted US8685984B2 Granted US8492386B2 Granted US8680048B2
Uruguay (UY)	Status: N/A UY32099A Status: N/A UY33981A Status: N/A UY35259A	Status: N/A UY32699A	Status: N/A[7] UY31344A1	Status: N/A UY33265A	Status: N/A UY33446A	Status: N/A UY34402A	Status: N/A UY34401A
Vietnam (VN)	Status: N/A VN13451A1	Status: N/A VN29908A	Status: N/A[7] VN24379A	N/A	Status: N/A VN201300076	N/A	N/A

	Patent 8	Patent 9	Patent 10	Patent 11	Patent 12	Patent 13	Patent 14
Subject Matter	Patent application WO2013040568 covers combination comprising paritaprevir, ritonavir and another anti-HCV agent.	Patent application WO2013101552 covers combinations of ombitasvir and other anti-HCV agents, useful for an interferon-free treatment of HCV infection.	Patent application WO2014004674 claims combination of an HCV protease inhibitor with ritonavir.	Patent application WO2014063101 claims a composition comprising pyrimidinedione derivative compounds and at least one bioavailability enhancing agent	Patent application WO2014011840 claims crystalline forms of paritaprevir.	Patent application WO2015002952 claims interferon-free therapy comprising paritaprevir and ombitasvir.	Patent application WO2015071488 claims composition comprising paritaprevir, ritonavir ombitasvir, which are co-formulated in an amorphous solid dispersion.
Applicant	AbbVie	AbbVie Inc.	AbbVie	AbbVie	AbbVie	AbbVie	AbbVie
Int'l Patent Publication Number	WO2013040568A1	WO2013101552	WO2014004674A2	WO2014063101A1	WO2014011840A1	WO2015002952A1	WO2015071488A1
Priority Number	US201161535550P	US2011580871P	US201261665019P	US201261715766P	US201261670905P	US201361842256P	US201361905537P US201361911784P
Expected expiry[1]	17 Sept 2032	17 Dec 2032	26 Jun 2033	18 Oct 2033	11 Jul 2033	01 Jul 2034	18 Nov 2034
PATENT STATUS							
ARIPO (AP)[2]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Argentina (AR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	Patent 8	Patent 9	Patent 10	Patent 11	Patent 12	Patent 13	Patent 14
Australia (AU)	N/A	N/A	N/A	Pending AU2013330993	N/A	N/A	N/A
Brazil (BR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Canada (CA)	Pending CA2847355A	N/A	Pending CA2876496A	Pending CA2888883A	Pending CA2878689A	N/A	N/A
Chile (CL)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
China (CN)	Pending CN103781496A	N/A	Pending CN104379145A	Pending CN104853752A	Pending CN104603138A	N/A	N/A
China, Hong Kong SAR (HK)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Colombia (CO)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Costa Rica (CR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ecuador (EC)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Egypt (EG)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ethiopia (ET)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
EAPO (EA)[3]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
EPO (EP)[4]	Pending EP2755689A	Pending EP2797594A	Pending EP2866807A	Pending EP2908808A	Pending EP2872513A	N/A	N/A
GCC[5]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Georgia (GE)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	Patent 8	Patent 9	Patent 10	Patent 11	Patent 12	Patent 13	Patent 14
India (IN)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Indonesia (ID)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Iran (Islamic Republic of) (IR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Israel (IL)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Japan (JP)	Pending JP2014530195A	N/A	Pending JP2015522022A	N/A	Pending JP2015522078A	N/A	N/A
Jordan (JO)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Malaysia (MY)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Mexico (MX)	Status: N/A MX2014003180A	N/A	N/A	N/A	Pending MX2015000535A	N/A	N/A
Morocco (MA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
New Zealand (NZ)	N/A	N/A	N/A	N/A	Pending NZ630435	Pending NZ630837	N/A
Nigeria (NG)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
OAPI[6]	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	Patent 8	Patent 9	Patent 10	Patent 11	Patent 12	Patent 13	Patent 14
Pakistan (PK)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Peru (PE)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Philippines (PH)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Republic of Korea (KR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Russian Federation (RU)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Singapore (SG)	N/A	N/A	N/A	Pending SG1120150305Q	N/A	N/A	N/A
South Africa (ZA)	N/A	N/A	N/A	Pending ZA201502615	N/A	N/A	N/A
Thailand (TH)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Tunisia (TN)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ukraine (UA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
The United States (US)	Abandoned US2013072528A Pending US20150025000A	Abandoned US20130172240A1	Pending US2014024613A	Pending US2014113921A	Pending US2014018518A	Pending US2015011481A	Pending US2015141351A

	Patent 8	Patent 9	Patent 10	Patent 11	Patent 12	Patent 13	Patent 14
Uruguay (UY)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Vietnam (VN)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	Patent 15	Patent 16	Patent 17	Patent 18	Patent 19	Patent 20
Subject Matter	Patent application WO2015084953 covers crystalline forms of paritaprevir.	Patent application WO2015103490 covers a dosage form comprising paritaprevir/ ritonavir/ ombitasvir/ dasabuvir.	Patent application WO2012009698 covers phosphine ligands useful for catalytic reactions.	Patent application WO2012009699 covers a process for preparing dasabuvir for use in HCV inhibition.	Patent application WO2014031791 covers processes for preparing dasabuvir or its salts for use in HCV inhibition.	Patent application WO2013106631A1 claims a process for the preparation of paritaprevir.
Applicant	AbbVie	AbbVie	AbbVie Inc. / Abbott Laboratories	Abbott Laboratories	AbbVie Inc.	AbbVie
Int'l Patent Publication Number	WO2015084953A1	WO2015103490A1	WO2012009698	WO2012009699	WO2014031791	WO2013106631A1
Priority Number	US201361911775P	US201461923544P US201461976934P	US2010365293P	US2010365293P	US13591117A	US201261585280P
Expected expiry[1]	03 Dec 2034	02 Jan 2035	14 Jul 2031	14 Jul 2031	20 Aug 2033	11 Jan 2033
PATENT STATUS						
ARIPO (AP)[2]	N/A	N/A	N/A	N/A	N/A	N/A
Argentina (AR)	N/A	N/A	N/A	N/A	N/A	N/A
Australia (AU)	N/A	N/A	Granted AU2011278926B2	Granted AU2011278927B2	N/A	N/A
Brazil (BR)	N/A	N/A	Status: N/A BR1120130011386	Status: N/A BR1120130011327	N/A	N/A
Canada (CA)	N/A	N/A	Pending CA2804827A1	Pending CA2805748A1	Pending CA2882624A	Pending CA2863002A
Chile (CL)	N/A	N/A	Status: N/A CL0146-2013	Pending[8] 0159-2013	N/A	N/A
China (CN)	N/A	N/A	Pending CN103097027A	Pending CN103097360A	Pending CN104884440	Pending CN104136453A

	Patent 15	Patent 16	Patent 17	Patent 18	Patent 19	Patent 20
China, Hong Kong SAR (HK)	N/A	N/A	Pending HK1184744	Pending HK1185078	N/A	Pending HK1201277
Colombia (CO)	N/A	N/A	Granted CO6710898A2	Status: N/A CO6670583A2	N/A	N/A
Costa Rica (CR)	N/A	N/A	Status: N/A CR20130057A	Status: N/A CR20130054A	N/A	N/A
Ecuador (EC)	N/A	N/A	N/A	Status: N/A SP2013-12348	N/A	N/A
Egypt (EG)	N/A	N/A	Pending[8] PCT79/2013	Status: N/A PCT78/2013	N/A	N/A
Ethiopia (ET)	N/A	N/A	N/A	N/A	N/A	N/A
EAPO (EA)[3]	N/A	N/A	Pending EA201390128A1	Pending EA201390130A1	N/A	N/A
EPO (EP)[4]	N/A	N/A	Pending EP2593226A1	Pending EP2593439A2	Pending EP2887941A1	Pending EP2802595A
GCC[5]	N/A	N/A	N/A	N/A	N/A	N/A
Georgia (GE)	N/A	N/A	N/A	N/A	N/A	N/A
India (IN)	N/A	N/A	Pending 276/DELNP/2013	Pending 638/DELNP/2013	N/A	N/A
Indonesia (ID)	N/A	N/A	Status: N/A IDWO201300629	Status: N/A IDWO00201300627	N/A	N/A
Iran (Islamic Republic of) (IR)	N/A	N/A	N/A	N/A	N/A	N/A
Israel (IL)	N/A	N/A	Pending IL224221	Pending IL224222	N/A	N/A
Japan (JP)	N/A	N/A	Pending JP2013534212A	Pending JP2013532636A	Pending JP JP2015526473	Pending JP2015508413A
Jordan (JO)	N/A	N/A	N/A	N/A	N/A	N/A
Malaysia (MY)	N/A	N/A	N/A	Pending[8] MYPI2013700083	N/A	N/A

	Patent 15	Patent 16	Patent 17	Patent 18	Patent 19	Patent 20
Mexico (MX)	N/A	N/A	Status: N/A MX2013000583A	Status: N/A MX2013000623A	N/A	Pending MX2014008516A
Morocco (MA)	N/A	N/A	N/A	N/A	N/A	N/A
New Zealand (NZ)	N/A	N/A	Granted NZ605471	Granted NZ605767 Pending NZ705225	N/A	N/A
Nigeria (NG)	N/A	N/A	N/A	N/A	N/A	N/A
OAPI[5]	N/A	N/A	N/A	N/A	N/A	N/A
Pakistan (PK)	N/A	N/A	N/A	N/A	N/A	N/A
Peru (PE)	N/A	N/A	Status: N/A PE20131095A1	Status: N/A PE20131086A1	N/A	N/A
Philippines (PH)	N/A	N/A	Pending PH12013500063	Pending PH 12013500105	N/A	N/A
Republic of Korea (KR)	N/A	N/A	Pending KR20130127428A	Pending KR2013043195A	N/A	N/A
Russian Federation (RU)	N/A	N/A	N/A	N/A	N/A	N/A
Singapore (SG)	N/A	N/A	Pending SG187103A1	Granted SG187102 Pending SG10201505540S	N/A	N/A
South Africa (ZA)	N/A	N/A	Granted ZA201300250	Pending ZA201300839	N/A	N/A
Tunisia (TN)	N/A	N/A	N/A	N/A	N/A	N/A
Thailand (TH)	N/A	N/A	Status: N/A TH1301000259	Status: N/A TH12013000260	N/A	N/A
Ukraine (UA)	N/A	N/A	Status: N/A UA201301880	Status: N/A UA201301879	N/A	N/A

	Patent 15	Patent 16	Patent 17	Patent 18	Patent 19	Patent 20
The United States (US)	Pending US2015175612A	Pending US2015258093A	Granted US8841487B2	Pending US20120014913A1	Pending US20130217876A1	Pending US2013178630
Uruguay (UY)	N/A	N/A	N/A	N/A	N/A	N/A
Vietnam (VN)	N/A	N/A	Pending VN2013/00250	Status: N/A VN34442A	N/A	N/A

[1] If granted and not subject to patent term extension.

[2] **The African Regional Intellectual Property Organization (ARIPO) includes the following countries:** Botswana, Ghana, Gambia, Kenya, Liberia, Lesotho, Malawi, Mozambique, Namibia, Sudan, Sierra Leone, Swaziland, the United Republic of Tanzania, Uganda, Zambia and Zimbabwe.

[3] **The Eurasian Patent Organization (EAPO) includes the following countries:** Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan and Turkmenistan.

[4] **The European Patent Office (EPO) includes the following countries:** Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Iceland, Italy, Liechtenstein, Lithuania, Luxemburg, Latvia, Malta, Monaco, Netherlands, Norway, Poland, Portugal, Romania, San Marino, Serbia, Slovenia, Slovakia, Spain, Sweden, Switzerland, The former Yugoslav Republic of Macedonia, Turkey and the United Kingdom.

[5] **The Patent Office of the Cooperation Council for the Arab States of the Gulf** (**Gulf Cooperation Council - GCC) includes the following countries**: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and United Arab Emirates.

[6] **The African Intellectual Property Organization (OAPI) includes the following countries:** Benin, Burkina Faso, Cameroon, Central African Republic, Chad, The Congo, Equatorial Guinea, Gabon, Guinea, Guinea Bissau, Côte d'Ivoire, Mali, Mauritania, Niger, Senegal and Togo.

[7] These patents/applications stems from WO2009/039127 instead of WO2009/039134.

[8] Information stems from the matching Form 3 of the respective patent filling in India. Please see the methodology section for further information.

GLOSSARY

INTERFERENCE PROCEEDING: An interference proceeding is a proceeding to determine the priority issues of multiple patent applications. Based on the (previous) first-to-invent system of the United States, a party which has failed to file a patent application on time is allowed to challenge the inventorship of another party which has a granted or pending patent.

N/A: N/A indicates that no information could be retrieved for the relevant patents in the databases that were used. This can either mean that the information in the databases is not up-to-date or complete, or that the patents were not filed in these jurisdictions. While the latter may often be the case, certainty can only be achieved by checking the information with the local patent office. This can be done by using the patent numbers provided in this report, as they allow retrieval of information through national patent offices and/or national patent registries

NOTICE OF ALLOWANCE: During a USTPO examination, if it appears to the examiner that the applicant is entitled to a patent under the law, a notice of allowance is sent to the applicant. The notice of allowance specifies a sum constituting the issue fee which must be paid within a given time from the date of mailing of the notice of allowance to avoid abandonment of the application.

PATENT FAMILY MEMBER: All patent publications that relate to the same basic patent (that is, invention) are members of this patent family. In the present study patent families are based on the Derwent World Patent Index (DWPI).

PENDING or GRANTED: Indicates a patent´s legal status.

PRIORITY NO: Earliest application number.

PUB NO: Patent publication number.

SPONSOR: The term “Sponsor” refers to the entities that are developing the medicines and are holding or filing for market authorization. Note that a Sponsor is not necessarily the patent assignee or applicant.

THE WIPO INTERNATIONAL SEARCH REPORT (ISR): After an applicant files a PCT application with WIPO, a search is conducted by an authorised International Searching Authority (ISA) to find the most relevant prior art documents regarding the claimed subject matter. The search results in an International Search Report (ISR), together with a written opinion regarding patentability.