# Title: Is Thailand’s hepatitis C treatment program at risk from its plans to join an Asia-Pacific trade pact?

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The authors declare no conflict of interest.

Ethics

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# Abstract

Thailand has expressed interest in joining the Comprehensive and Progressive Agreement for Trans-Pacific Partnership (CPTPP), an 11-country plurilateral trade agreement whose original incarnation included the United States of America (USA). When the USA withdrew from this agreement, key intellectual property clauses relevant to pharmaceuticals were suspended. These could be reinstated should the USA decide to re-join. This study aimed to measure the impact of these suspended clauses by costing Thailand’s 2020 hepatitis C treatment program under four scenarios: 1) existing treatment regime, which does not use the currently recommended treatment regime and does not source the lowest price medicines, 2) treatment regime if Thailand joined the CPTPP and suspended clauses were reinstated, 3) treatment regime if Thailand utilised flexibilities in international law enabling access to the cheapest direct acting antivirals on the global market and 4) lowest-cost generic pan-genotypic regime on the global market. Joining the CPTPP would increase the cost of Thailand’s hepatitis C treatment program more than tenfold if suspended CPTPP clauses were reinstated and TRIPS flexibilities not fully utilised. Within the existing budget, the price and regime for scenario 4 would enable an additional 7,571 people to access hepatitis C treatment and avoid the need for genotype testing. Signing trade agreements such as the CPTPP that require stronger intellectual property protections could compromise Thailand’s hepatitis C program and other national treatment programs reliant on affordable generic medicines and prevent it from relying on its own pharmaceutical capabilities to manufacture medicines needed to sustain its treatment programs.

# Highlights

* Thailand has expressed interest in joining the CPTPP trade agreement, an eleven-country plurilateral trade agreement signed in 2018
* The CPTPP contains (currently suspended) intellectual property clauses relevant to pharmaceuticals which could have implications for access to affordable hepatitis C medications
* Thailand should reject joining the CPTPP due its potential impact on not only the cost of the hepatitis C program but all national treatment programs reliant on affordable generic medicines.

# Keywords

Intellectual property, patents, generic medicines, compulsory licencing, TRIPS flexibilities, trade agreements, TRIPS-plus, hepatitis C, direct-acting antivirals.

# Main text

# Introduction and background

Thailand has expressed interest in joining the Comprehensive and Progressive Agreement for Trans-Pacific Partnership (CPTPP), an 11-country plurilateral trade agreement signed in 2018 between Australia, Brunei Darussalam, Canada, Chile, Japan, Malaysia, Mexico, Peru, New Zealand, Singapore and Vietnam. This research aims to measure the potential impact of signing this agreement on access to medicines in Thailand, specifically the impact of its intellectual property (IP) provisions on access to direct acting antivirals (DAA) used to treat hepatitis C.

## Thailand’s Economic Situation

Thailand has made significant strides in socio-economic development, moving from a low-income to an upper-middle income country (as defined by The World Bank) in less than a generation (1). It has experienced strong economic growth and marked poverty reduction.

## Implications of Thailand’s membership of the World Trade Organization

The WTO’s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) came into effect on 1 January 1995 and remains the most comprehensive multilateral agreement on intellectual property (IP) (2, 3). As a WTO Member State, Thailand must comply with TRIPS and provide minimum standards of IP protection, including making patents of at least 20 years available for pharmaceutical products or processes that meet standard criteria for patentability, novelty, inventive step and industrial applicability (4).

## Thailand’s Use of Flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights

Together with Ecuador, Thailand has made the most frequent use of TRIPS flexibilities (5) which are designed to mitigate the negative impacts of patents, such as high medicine prices. Compulsory licenses are an important example of TRIPS flexibilities (6). TRIPS article 31 defines a compulsory licence as an authorisation granted by a government that allows the government or a third party to produce a patented product or to use a patented process without the consent of the patent holder (6). The patent holder must be paid a royalty based on the percentage of sales. (7).

Thailand has issued seven government for public non-commercial use compulsory licences in total. In 2006, the Government of Thailand issued a compulsory licence for the anti-retroviral (ARV) medicine efavirenz. In 2007 it issued compulsory licences for the second-line ARV combination of lopinavir/ritonavir (LPV/r), marketed as Kaletra by Abbott Laboratories and clopidogrel (an antiplatelet agent used in the treatment of stroke and coronary artery disease) (8). This was the first time a developing country had issued a compulsory licence for a medicine other than an ARV. Four additional compulsory licenses were granted in 2008 by the Government of Thailand for letrozole (for breast cancer (9)), docetaxel (for breast, head and neck, stomach, prostate and non-small-cell lung cancer) (10), erlotinib (for lung and pancreatic cancer) (11) and imatinib (for leukaemia) (12).

## Intellectual Property law in Thailand

Thailand passed the Patent Act B.E. 2522 in 1979 (13). This has been amended twice; first in 1992, due to pressure on Thailand from the United States of America (USA) to increase patent protection for US pharmaceutical companies (14). This amendment included patents for pharmaceutical products, increased the patent protection period from filing from 15 to 20 years and added a pre-grant opposition procedure. The second amendment occurred in 1999 to comply with the TRIPS Agreement. It narrowed the grounds for compulsory licences and abolished The Drug Board, a government agency set up in 1992 to control medicine prices and prevent pharmaceutical industry monopolies.

Thailand’s Trade Secret Act 2545 (2002) (amended in 2015 to be Trade Secret Act 2558) provides protection against breaches of confidentiality and unfair commercial use for five years for test data and other information submitted to the Thai Food and Drug Administration (FDA) in dossiers for pharmaceuticals (15). This form of data protection does not prevent the FDA from relying on the data to assess and approve applications for generic medicines. The 2007 Ministerial Regulation Regarding Trade Secrets further specifies that this data protection only applies to new medicines with a new chemical entity and is not available for new biologics, new formulations of existing medicines and new uses/indications (16).

## Thailand’s interest in the TPP and CPTPP

Thailand has repeatedly expressed interest in joining the CPTPP (17). Membership of the CPTPP is seen by many in the Thai government as a demonstration of international relevance and a conduit to joining future FTAs as well as an opportunity to boost exports, attract foreign direct investment (FDI), and create jobs (18).

The Trans-Pacific Partnership Agreement (TPP) was a proposed trade agreement between Australia, Brunei, Canada, Chile, Japan, Malaysia, Mexico, New Zealand, Peru, Singapore, Vietnam, and the United States. It was signed in February 2016, and had not been ratified when President Donald Trump withdrew the United States in January 2017. The remaining 11 countries negotiated a new trade agreement called CPTPP, which incorporates most of the provisions of the TPP, and entered into force on 30 December 2018.

The TPP included an IP chapter with multiple provisions shown to have a negative impact on access to medicines (19). After the US withdrawal, several of these provisions were suspended including IP provisions that go beyond the requirements of the TRIPS Agreement (TRIPS-plus provisions). These suspended provisions could be reintroduced by agreement amongst the parties if the Biden Administration decides to re-join this Agreement (20). The suspended provisions are explained in Table 1 below.

Not all TRIPS-plus provisions were suspended. For example, the CPTPP retained TPP Article 18.53 which provides for patent linkage. This is a conditional relationship between the granting of marketing approval for a generic medicine and the patent status of the originator medicine. The CPTPP allows for two different approaches to patent linkage. The first, described in Art. 18.53 para 1, requires a system to alert the rights holder when a third party is seeking to market a product covered by a patent, and the provision of a judicial or administrative process for resolving disputes. The second alternative (Art 18.53 para 2) requires direct coordination between the marketing approval authority and the patent office, and an automatic stay on marketing approval where a patent may be infringed. The two options allow Thailand some flexibility in implementing patent linkage in a way that mitigates its impact on the market entry of generics. However, a health impact assessment found that implementing patent linkage could negatively affect the domestic pharmaceutical industry in Thailand and increase its reliance on imported medicines (21).

The CPTPP text also includes a footnote to Article 18.37 paragraph 1 which establishes a lower threshold for inventiveness than is required by TRIPS:

30 For the purposes of this Section, a Party may deem the terms ‘inventive step’ and ‘capable of industrial application’ to be synonymous with the terms ‘non-obvious’ and ‘useful’, respectively. In determinations regarding inventive step, or non-obviousness, each Party shall consider whether the claimed invention would have been obvious to a person skilled, or having ordinary skill in the art, having regard to prior art. (CPTPP Chapter 18, Footnote 30)

This provision, particularly the reference to a person “having ordinary skill in the art” (which is TRIPS-Plus) can result in the granting of poor-quality patents (22). Although the Thai Patent Act (No.3) B.E. 2542 includes a similarly low inventiveness threshold, Thailand currently has the policy space to lift the threshold. Membership of the CPTPP would remove this element of discretion, creating a binding obligation to retain the low inventiveness threshold.

**Table 1: Suspended TRIPS-plus IP articles of the CPTPP**

|  |  |
| --- | --- |
| **Suspended Article** | **Explanation** |
| Article 18.37 (Patentable Subject Matter)  (i) paragraph 2: all of this paragraph;  (ii) paragraph 4: the last sentence; | Patents to be made available for at least one of: new uses of a known product, new methods of using a known product or new processes of using a known product. Patents must be available for inventions derived from plants. |
| Article 18.46 (Patent Term Adjustment for Unreasonable Granting Authority  Delays): all of this Article including footnotes 36 through 39; | Adjust, upon request, a patent's term of protection to compensate the patent owner if there are unreasonable delays in a patent office's issuance of a patent. |
| Article 18.48 (Patent Term Adjustment for Unreasonable Curtailment): all of  this Article including footnotes 45 through 48; | Adjust a pharmaceutical patent's term of protection to compensate the patent owner for unreasonable curtailment of the effective term of a patent as a result of the marketing approval process for a pharmaceutical product. |
| Article 18.50 (Protection of Undisclosed Test or Other Data): all of this  Article including footnotes 50 through 57; | At least five years of exclusivity for test or other data submitted to a regulatory agency to prove the safety and efficacy of a new medicine. |
| Article 18.51 (Biologics): all of this Article including footnotes 58 through 60; | At least eight years of effective market protection for biologics, provided via at least 8 years of data exclusivity or at least 5 years of data exclusivity and other measures to ‘deliver a comparable outcome in the market’. |

Adapted from Comprehensive and Progressive Agreement for Trans-Pacific Partnership text. See <https://www.dfat.gov.au/sites/default/files/tpp-11-treaty-text.pdf>

Most of the higher-income countries in the CPTPP already have provisions in their patent law that reflect these suspended clauses. The impact of these currently suspended provisions would therefore be felt most keenly in lower-income countries which are already the least able to provide affordable access to medicines for their populations (19).

With the Trump administration no longer in power, the USA may wish to re-join the CPTPP. If it does re-join, some or all of the suspended clauses may be reinstated, and all Member countries would need to ensure their domestic legislation is compliant.

It is important to note, however, that the CPTPP IP chapter does not place restrictions on compulsory licensing. Article 18.6 of the TPP, retained in the CPTPP, reaffirms each party’s right to take measures to protect public health and to use TRIPS flexibilities (23). The final text of the data exclusivity provision of the TPP included an exception (Article 18.50 paragraph 3, which also applies to Article 18.51 for biologics) for measures to protect public health in accordance with the Declaration on TRIPS and Public health. This means CPTPP signatories should be able to incorporate exceptions from data exclusivity for compulsory licensing in their domestic laws without breaching the CPTPP even if the data exclusivity provisions are reinstated.

While the CPTPP IP chapter does not create obstacles to compulsory licensing, it is possible that its investment chapter may. Intellectual property rights are recognised as covered investments in Article 9.1 of the Investment Chapter, and investors may use the CPTPP’s investor-state dispute settlement (ISDS) mechanism to initiate arbitration in an international tribunal when they believe their investor rights under the agreement have been breached (24). Article 9.8 para 5 provides an exception to the expropriation provisions for compulsory licenses that are compliant with the CPTPP IP chapter and the TRIPS Agreement, but it is possible that this (as yet untested) exception may not be sufficiently robust, or that an ISDS case over compulsory licensing could be initiated using the investment chapter’s provisions for ‘fair and equitable treatment’ (Article 9.6) (24). Scholars have raised concerns about the robustness of several exceptions in the investment chapter, including the exception in Annex 9-B para 3(b) which excludes ‘non-discriminatory regulatory actions…that are designed and applied to protect legitimate public welfare objectives, such as public health, safety and the environment…’ from claims regarding indirect expropriation, ‘except in rare circumstances’ (25, 26).

Provisions in other CPTPP chapters have implications for various aspects of pharmaceutical policy, (27) however these are beyond the scope of the current paper, which focuses on the impact of the CPTPP’s IP provisions.

## Hepatitis C infection and treatment

Hepatitis C is a blood borne virus that if untreated, can lead to liver damage, liver cancer and sometimes death.

WHO’s global hepatitis strategy, The Global Health Sector Strategy, endorsed by all WHO Member States including Thailand, aims to reduce new cases of chronic HCV infection by 90%, decrease HCV-associated mortality by 65%, and treat 80% of chronic HCV infection by 2030 (28). Despite progress against the 2020 hepatitis targets, the gaps towards achieving 2030 goals are huge (29). Infection with hepatitis C does not always require treatment, as some people’s immune response will clear the infection. If this does not happen and the infection becomes chronic, treatment is necessary to avoid liver damage and sequalae including liver cancer (30). In the past decade, the introduction of direct-acting antiviral (DAA) medicines has revolutionized hepatitis C treatment, demonstrating high efficacy and good tolerability. Previous treatment for hepatitis C had consisted of injectable pegylated interferon alpha and oral ribavirin. This treatment was less efficacious than the DAA and took up to a year (31) compared with 8-24 weeks with the use of DAAs (see Table 2). Side effects in some people were severe and commonly resulted in default from treatment (32).

HCV has six genotypes named 1 to 6. People infected with genotype 1 may have a greater chance of developing cirrhosis, or severe liver scarring, than from other genotypes. Genotypes 1b and 3 may increase the risk of liver cancer (33).

WHO recommends therapy with pan-genotypic DAA (i.e., those that can be used for all genotypes) for persons over the age of 12 years. DAAs can cure 90% or more of people with HCV infection and treatment duration is short (usually 8 to 24 weeks), depending on the absence or presence of cirrhosis (30). WHO treatment guidelines for adults are detailed in Table 2.

**Table 2 WHO hepatitis C treatment guidelines for adults 2018**

|  |  |  |
| --- | --- | --- |
| HCV positive patients | Treatment combination | Treatment duration |
| Patients > 18 years without cirrhosis | Glecaprevir/Pibrentasvir | 8 weeks\* |
| Sofosbuvir/daclatasvir | 12 weeks |
| Sofosbuvir/velpatasvir | 12 weeks |
| Patients > 18 years with compensated cirrhosis | Glecaprevir/Pibrentasvir | 12 weeks\* |
| Sofosbuvir/daclatasvir | 24 weeks |
| Sofosbuvir/daclatasvir | 12 weeks\*\* |
| Sofosbuvir/velpatasvir | 12 weeks |

\* Persons with HCV genotype 3 infection who have received interferon and/or ribavirin in the past should be treated for 16 weeks.

\*\* May be considered in countries where genotype distribution is known and genotype 3 prevalence is <5%.

Adapted from the WHO hepatitis C treatment guidelines 2018

Sofosbuvir, a DAA produced by Gilead Sciences (hereafter, Gilead) and marketed as Sovaldi, was first launched in 2014 for a price that made it unaffordable to most people even in high-income countries. A 12-week combination treatment with a sofosbuvir-based regimen ranged from US$84,000 to $94,000 or approximately US$1000 per pill (34). In its first year on the market, Sovaldi generated $US10.3 billion in sales for Gilead and came close to being the highest revenue producing medicine in the world (35). In contrast, a study from 2014 estimated the manufacturing costs of a 12-week course of sofosbuvir to be US$68–US$136 (36).

## Medicines Patent Pool (MPP) licences

The MPP is a United Nations-backed public health organisation working to increase access to, and facilitate the development of, life-saving medicines for LMIC. MPP partners with civil society, governments, international organisations, industry, patient groups, and other stakeholders, to prioritise and facilitate voluntary licenses for priority medicines and pool intellectual property to encourage generic manufacture and the development of new formulations (37).

Most agreements facilitated and signed by MPP are for ARVs, however MPP has also signed agreements with three patent holders for three hepatitis C DAAs; Daclatasvir (DAC) Glecaprevir/pibrentasvir (G/P) and Ravidasvir (RAV) (38). They are detailed in Supplementary file 1.

Thailand is not included in any of the three DAA MPP agreements given it is an upper-middle income country and the MPP is focused primarily on increasing access to medication in LMIC. In March 2020, Bristol-Myers Squibb (BMS) announced that it would not enforce patents on Daclatasvir in countries where the product is no longer routinely prescribed or where there are other therapeutic options available. Thailand was included among these countries. Additionally, BMS will discontinue Daklinza, its originator brand of daclatasvir in those same countries. The BMS and the AbbVie MPP Agreements allow countries not included in the licence to be supplied by MPP licensees provided no patent is being infringed (39).

## Bilateral licences

In 2014 Gilead issued voluntary licences to manufacture sofosbuvir directly to 11 generic manufacturers in India, allowing generic versions of its DAAs to be sold in over 100 countries. This agreement excluded Thailand and a number of middle-income countries with high burdens of HCV (40). In August 2017, Gilead expanded the territory of its license to include Belarus, Malaysia, Thailand and Ukraine. This followed Malaysia’s decision to issue a compulsory license for sofosbuvir following failed price negotiations with Gilead and attempts to be included in the original voluntary licence (41).

## Hepatitis C in Thailand

Approximately 760,000–790,000 people in Thailand are HCV seropositive and about half are living with chronic infection (42, 43). Although genotype 1 is the most prevalent in the western world (44), genotype 3 is most common in Thailand at 46.1%, followed by genotypes 1, 6 and 2 at 32.5%, 20.9%, and 0.5%, respectively (45).

Thailand began providing treatment for HCV with DAAs free of charge in the government health care system in 2018. Due to cost and resource constraints DAAs were not available for several years to all people living with HCV and some older peg-interferon and ribavirin based therapies were used (46). Treatment regimens were not pan-genotypic and therefore required genotype testing which adds to the treatment costs. Treatment was limited to a small number of people with chronic HCV due to stringent eligibility criteria (47). These regimens are detailed in Table 3.

**Table 3: Thai government reimbursement scheme hepatitis C treatment regimens in 2020**

|  |  |  |
| --- | --- | --- |
| Hepatitis C genotype | Treatment regime | Length of treatment |
| 3 | SOF+Peg-IFN+RBV combination therapy | 12 weeks |
| 1, 2, 4, and 6 without liver cirrhosis | SOF+LDV combination therapy | 12 weeks |
| 1, 2, 4, and 6 with liver cirrhosis | SOF+LDV+RBV combination therapy | 12 weeks |

Adapted from Sirinawasatien A, Techasirioangkun T. Sofosbuvir-based regimens in the treatment of patients with chronic hepatitis C virus infection: Real-world efficacy in Thailand. PLoS One. 2020 Feb 27;15(2):e0229517

SOF= Sofosbuvir, LDV= Ledipasvir, RBV= Ribavirin , Peg-IFN= Pegylated interferon

In 2020, SOF and SOF/LDV were sourced from the Indian generic company, Mylan. Ribavirin and peg-interferon were sourced from Merck Sharp & Dohme and Roche respectively (46).

## Patent status of DAAs in Thailand

Many patent applications have been filed for DAAs in Thailand. All patent applications are pending and many patents for DAAs, including sofosbuvir, have been opposed by patient groups and NGOs on the grounds that they lack novelty and an inventive step (48). These are detailed in supplementary file 2.

Hepatitis C remains a significant health burden in Thailand. To address this issue requires considerable scale up of testing and treatment. Thailand has the industrial capacity to manufacture generic DAAs in country making treatment more affordable and sustainable. The advent of DAAs has revolutionised hepatitis C treatment but they are mostly patented and expensive. The Thai national hepatitis C treatment program therefore provides a case study to explore the impact of TRIPS-plus trade agreements on access to affordable medicines.

# Aims

This study aims to determine the potential impact on Thailand’s hepatitis C treatment program if Thailand decides to join the CPTPP and all suspended IP clauses are reinstated. Impact is measured as the cost of the treatment program and the number of people able to access treatment.

# Methods

## Scenario development

Four scenarios were designed to explore the potential impacts of joining the CPTPP on Thailand’s hepatitis C treatment program:

* Scenario 1 (baseline): This scenario involves Thailand’s current patent law, the 2020 hepatitis C treatment regime and no issuance of compulsory licenses for hepatitis C medicine.
* Scenario 2: In this scenario, Thailand joins the CPTPP, suspended clauses are reinstated, and the 2020 hepatitis C treatment regime is used. No compulsory licenses are issued for hepatitis C medicines.
* Scenario 3: This scenario involves full use of TRIPS flexibilities, i.e., issuance of compulsory licenses for all medicines where patents would otherwise present barriers to access (irrespective of whether Thailand joins CPTPP or not).
* Scenario 4: This involves Thailand’s current patent law, the lowest price generic WHO recommended pan-genotypic regime, and no issuance of compulsory licenses for hepatitis C medicines.

These scenarios were chosen to encompass the range of policy options available to Thailand and the impact of each of these options on the cost of the hepatitis C treatment program as a comparator to the CPTPP scenario. Relevant international and Thai IP and access to medicines experts were consulted to ensure that the study focused on the most pertinent trade agreement for Thailand was included, that there was an expert understanding of current patent law and that the relevant range of options were being explored.

To finalise Scenario 2 and its assumptions, it was necessary to determine if the CPTPP and its suspended clauses would require legislative change in Thailand, should they be reinstated. Relevant Thai legal text was examined for compliance with patent linkage and CPTPP suspended IP clauses**.** See Table 4 for possible legislative changes and Table 1 for an explanation of the clauses.

**Table 4: CPTPP suspended clauses and possible legislative change required in Thailand**

|  |  |
| --- | --- |
| **CPTPP suspended clauses and existing patent linkage clause** | **Corresponding clauses that would require legislative change** |
| Article 18.37: Patentable Subject Matter  Suspend Paragraph 2 and Paragraph 4, second sentence | Thai Patent Act Section 9. The following inventions are not protected under this Act:  **(4) methods of diagnosis, treatment or cure of human and animal diseases;** |
| Article 18.46: Patent Term Adjustment for Unreasonable Granting Authority Delays  Article 18:48: Patent Term Adjustment for Unreasonable Curtailment | Thai Patent Act Part III Rights Conferred by the Patent 35(14). An invention patent shall **have a term of twenty years from the date of filing of the application in the country**. |
| Article 18.50: Protection of Undisclosed Test or Other Data | Trade Secret Act B.E.2558 |
| Article 18.51: Biologics | **Trade Secret Act B.E 2558** |
| Article 18.53: Patent Linkage | Drug Act (No. 6) B.E. 2562 and its Regulation on marketing approval process |

Adapted from Comprehensive and Progressive Agreement for Trans-Pacific Partnership text and Thai legal text. See <https://www.dfat.gov.au/sites/default/files/tpp-11-treaty-text.pdf>

The cost of the DAAs[[1]](#footnote-1) in Thai hepatitis C program were then calculated for each of the four scenarios. See Table 5 for the scenarios and their related assumptions.

**Table 5: Scenarios for costing DAA in hepatitis C treatment program**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Scenario 1 - Baseline** – **2020 treatment regime** | **Scenario 2- Thailand joins CPTPP (suspended clauses are reinstated)** | **Scenario 3- full use of TRIPS flexibilities (irrespective of whether Thailand joins CPTPP or not)** | **Scenario 4- Lowest price generic WHO recommended pan-genotypic regime** |
| **Regime** | * SOF/LDV for genotype 1,2,4,6 * SOF for genotype 3 * Genotype test | * SOF/LDV for genotype 1,2,4,6 * SOF for genotype 3 * Genotype test | * SOF/LDV for genotype 1,2,4,6 * SOF for genotype 3 * Genotype test | * SOF/VEL * No genotype test required |
| **Assumptions** | * Generic DAA regimes used in Thailand in 2020; * Uses Mylan generic price for Thailand in 2020; * Treatment for genotypes 1,2,4,6 use the DAA regime of SOF/LDV; * Treatment of people with HCV-3 is with SOF and Pegylated interferon and Ribavirin combination therapy. Only the SOF (DAA) component of this is costed; | * Assumes patents are granted for all filed secondary patent applications as CPTPP allows for secondary patenting. (Patents to be made available for at least one of: new uses[[2]](#footnote-2) of a known product, new methods of using a known product or new processes of using a known product); * Patent terms may be extended due to CPTPP patent term extensions; * Data exclusivity and patent linkage may further delay marketing approval and/or market entry for generics; * Treatment for genotypes 1,2,4,6 use the DAA regime of SOF/LDV; * Treatment of people with HCV-3 is with SOF and Pegylated interferon and Ribavirin combination therapy. Only the SOF (DAA) component of this is costed; | * Compulsory licences are granted for all patented medicines and Thailand can therefore access the least expensive SOF/LDV and SOF on the global market; * Treatment for genotypes 1,2,4,6 use the DAA regime of SOF/LDV; * Treatment of people with HCV-3 is with SOF and Pegylated interferon and Ribavirin combination therapy. Only the SOF (DAA) component of this is costed; | * Thailand is able to access the least expensive generic SOF/VEL on the market as no current patents have been granted and it is not locked into a voluntary licence agreement; * This scenario is not permissible if Thailand signs onto CPTPP as it will need to grant secondary patents (unless compulsory licensing is invoked); * No genotype testing required as it is a pan genotypic regime; * Measuring the DAA in this scenario calculates the full cost of treatment unlike scenario 1-3. |

VEL= Velpatasvir

None of the scenarios above include hepatitis C treatment for people with liver cirrhosis. Scenario 1, 3 and 4 are policy options available to Thailand without the need of legislative change. Scenario 2 would require legislative change as outlined in table 4.

## Data collection

The number of people treated with DAAs for hepatitis C in Thailand in 2020 was sourced from Thai National Health Security Office (NHSO) and was a constant for all four scenarios. The price data for Scenario 1 was sourced from NHSO. Price data for Scenario 2 and genotype testing prices were obtained from the Health Intervention and Technology Assessment Program (HITAP) study by Rattanavipapong et al: “Revisiting policy on chronic HCV treatment under the Thai Universal Health Coverage: An economic evaluation and budget impact analysis”[[3]](#footnote-3) `(49). Price data for Scenario 3 and 4 were sourced from the WHO publication “Accelerating access to hepatitis C diagnostics and treatment: Overcoming barriers in low and middle-income countries – Global progress report 2020”(50).

## Data analysis

For each scenario, the total cost of DAA in hepatitis C treatment was calculated by multiplying the cost of the relevant DAA regime (including the genotype test where relevant) per person by the number of people being treated using that regime for the year 2020.

# Results

The full cost of each scenario is detailed in Table 6

**Table 6: Cost of DAA in hepatitis C treatment in scenarios in US$**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Cost of DAA regime/test per person (US$)** | **Number of people treated** | **Total cost of DAA regime/genotyping by number of people treated** |
| **Scenario 1** | | | |
| SOF/LDV for genotype 1,2,4,6 | 349 | 1993 | 695,557 |
| SOF for genotype 3 | 293 | 1372 | 401,996 |
| Genotyping | 161.4 | 3365 | 543,111 |
| Pharmaceutical company producing medication | Mylan | | |
| Total cost of DAA in hepatitis C treatment | **1,640,664** | | |
| **Scenario 2** | | | |
| SOF/LDV for genotype 1,2,4,6 | 5323 | 1993 | 10,608,739 |
| SOF for genotype 3 | 4028 | 1372 | 5,526,416 |
| Genotyping | 161.4 | 3365 | 543,111 |
| Pharmaceutical company producing medication | Gilead | | |
| Total cost of DAA in hepatitis C treatment | **16,678,266** | | |
| **Scenario 3** | | | |
| SOF/LDV for genotype 1,2,4,6 | 120 | 1993 | 239,160 |
| SOF for genotype 3 | 60 | 1372 | 82,320 |
| Genotyping | 161.4 | 3365 | 543,111 |
| Pharmaceutical company producing medication | Mylan, Hetero and Strides Shasun | | |
| Total cost of DAA in hepatitis C treatment | **864,591** | | |
| **Scenario 4** | | | |
| SOF/VEL for all genotypes | 150 | 3365 | 504,750 |
| Pharmaceutical company producing medication | Mylan | | |
| Total cost of DAA in hepatitis C treatment | **504,750** | | |

Scenario 4 (the lowest price generic WHO recommended pan-genotypic regime) is the lowest cost scenario at US$504,750. This is approximately three times less expensive than the baseline cost of DAA treatment in Thailand outlined in Scenario 1. Scenario 2 (Thailand joins CPTPP and suspended clauses are reinstated) is the most expensive scenario and more than ten times the cost of the baseline DAA treatment program. Despite Scenario 3 making use of TRIPS flexibilities, it is not the cheapest option as it uses a non-genotypic regime and therefore has to include the cost of genotype testing. Scenario 3 is however, less expensive than the baseline in Scenario 1. Scenario 4 is the cheapest option and an even less expensive option for Thailand than it appears given it measures the full cost of hepatitis C treatment and not only the partial cost. This difference is because scenarios 1-3 only cost the DAA component and not the pegylated interferon/ribavirin component in use. The budget of US$1,640,644 outlined in scenario 1, and the price and regime outlined in scenario 4, would fund an additional 7,571 people to access hepatitis C treatment or 3.2 times the number of people being treated with DAAs in 2020.

# Discussion

The cost of scenario 2 clearly demonstrates the potential implications for the cost of DAAs if Thailand decides to join the CPTPP and the suspended clauses are reinstated. The CPTPP’s suspended clauses allow for secondary patenting and patent term extensions. These clauses would facilitate the granting of secondary DAA patents currently pending and opposed by patient groups. See supplementary file 2 for a list of primary and secondary patent applications for SOF, LDV and VEL in Thailand. The list of secondary patent applications includes, but is not limited to, sofosbuvir crystalline forms & preparation processes and sofosbuvir processes & intermediates. There would be little to no grounds for patent opposition if secondary patenting was possible. Thailand’s Patent Act allows for pre-grant opposition which offers third parties an opportunity to oppose the grant of a patent within 90 days of the patent application (13). They must demonstrate that the application does not meet patentability requirements. Grounds for opposition would be narrowed if patentability standards were lowered to allow patents for new uses of a known product, new methods of using a known product or new processes of using a known product.

Voluntary licences can substantially improve access to HCV treatment in countries included in such agreements, by improving the affordability and supply of generic products and have been lauded as a practical way to overcome the barriers that patents pose such as high prices (51). They have however been criticised for their lack of transparency and restrictive conditions that can undermine access to medicines (41). When a patent is granted in a country, the ability of a country such as Thailand to access an affordable generic can be contingent on the terms and conditions of the voluntary licence in play (50). All three DAA MPP licences exclude Thailand and many other middle-income countries which account for the majority of the global burden of hepatitis C infection. The BMS and the AbbVie MPP Agreements allow countries not included in the licence to be supplied by MPP licensees provided no patent is being infringed. However, as there are no Thai DAA patents, Thailand is unencumbered in seeking the best generic price on the global market which may or may not include those from the MPP licensees. Scenario 1 demonstrates that voluntary licensees do not necessarily provide the least expensive generic option.

Additionally, it was only after Malaysia made use of TRIPS flexibilities and issued a compulsory licence for SOF that Gilead extended its bilateral licence to include Thailand and several other high burden middle-income countries. The compulsory licence allowed Malaysia to import a generic at a cheaper price than the generic companies included in the voluntary licence (52). Although Gilead’s bilateral licence appears broad and far-reaching it only allows for eleven Indian, one Pakistani and two Egyptian generic companies to produce and sell SOF (53). Thailand has an established pharmaceutical manufacturing industry with the capacity to manufacture a range of pharmaceuticals including DAAs. The Government Pharmaceutical Organization (GPO) is a wholly government-owned enterprise that has long supplied the majority of ARVs for the national HIV treatment program (54). Limiting the bilateral licence to include only Indian generic companies prohibits Thailand from using its own production capacity which is likely to be less expensive and less reliant on global supply chains. It is anticipated that the GPO will obtain marketing approval for its generic SOF/VEL in late 2022 and at that point, local production and increased generic competition will bring down the price of SOF/VEL (55). The bilateral licence has created a pseudo-monopoly for Indian companies included in the licence and empowered them to charge non-competitive prices especially if only one of the companies decides to register in a country, as is the case with Thailand. Despite the bilateral agreement in place and no patents on DAAs, Thailand still paid significantly more for generic SOF than the lowest price generic available as demonstrated by scenario 1 versus scenario 3.

Currently, as there are no patents granted for DAAs in Thailand, it is not locked into paying high prices for patented DAAs nor is it confined to the terms of Gilead’s bilateral licence. It is perplexing why Thailand was paying high generic prices when it could have been sourcing much cheaper pan- genotypic regimes that do not require genotype testing, saving both time and money. It was also using a superseded regime (pegylated interferon and ribavirin) that is no longer recommended by WHO, has a longer treatment duration, is less efficacious and is associated with significant side effects.

Scenario 4 includes a generic pan-genotypic regime that is recommended by WHO and does not require genotype testing. It is the least expensive, most effective treatment option with the fewest side effects available to Thailand. Thailand has provided this option since January 2021 using sofosbuvir and velpatasvir (SOF/VEL) generics from Mylan, although access is reported to be complicated by eligibility criteria, requirements for pre-treatment diagnostic tests, and the need for specialist administration of HCV treatment (55). It is encouraging that Thailand has now adopted a pan-genotypic treatment regime, however the ability to continue to access this product at this price could be impacted if a patent is granted.

If Thailand joined the CPTPP, the Agreement could potentially lock it into paying high prices for patented DAAs and or limit Thailand to buying from Indian generic companies included in bilateral pharmaceutical voluntary licences. This arrangement would compromise its purchasing power and restrict Thailand from producing its own DAAs, which it has the industrial capacity to do. Joining the CPTPP does not restrict Thailand’s ability to issue a compulsory licence to access cheaper generics and so this remains a viable option, however it is possible that Thailand could face ISDS disputes over compulsory licenses. Compulsory licensing is often an onerous and tedious process and comes with its own challenges. Thailand faced enormous backlash from the USA and pharmaceutical company Abbott Laboratories when it issued seven compulsory licences in the past. Following the licences, the USA placed Thailand on the United States Trade Representative (USTR) Priority Watch List under Special 301 of the Omnibus Trade and Competitiveness Act of 1988. It also threatened to rescind the trade privileges granted to Thailand under the Generalised System of Preferences (56). Abbott refused to register any new medicines in Thailand and withdrew any medicines it had awaiting registration (57). This may make Thailand hesitant to pursue this option.

# Limitations

Scenarios 1-3 did not calculate the full cost of treatment, only the cost of the DAA component for the reason mentioned in footnote 1. The 2020 Thai treatment regime for genotype 3, the most common HCV genotype in Thailand, required treatment with pegylated interferon and ribavirin on the basis of cost. However, this treatment is no longer recommended by the WHO and has been superseded by pan-genotypic DAA. Therefore, treatment costs of scenarios 1-3 are underestimates whereas scenario 4 calculates the complete cost of hepatitis C (all genotypes) treatment.

In contrast to retrospective studies, prospective studies of the impact of trade agreements tend to find larger negative effects of stronger IP provisions on prices and costs of medicines (58). As this is a prospective analysis, it is possible that assumptions made in this study overestimate the likely impact of the CPTPP.

In addition, this cross-sectional study measured only the most immediate impacts of the CPTPP if Thailand joined and the suspended clauses were reinstated. Some of the suspended CPTPP TRIPS-plus provisions and the patent linkage provision will have more cumulative effects over time and their impact on the price of medicines will not be realised for years to come (59). Further research is needed to better understand the impact of patent linkage, patent term extensions and data exclusivity.

It is possible that Thailand will decide not to join the CPTPP. It is also possible that Thailand will join, and the USA will decide not to re-join and therefore the suspended clauses will not be reinstated in their original form. The scenarios featured in this study therefore are only valid for the specific set of circumstances described.

The results of this study are limited to the impact on DAAs only and findings are not necessarily generalisable to other medicines. Additionally, this study only analyses the impact of the IP provisions and not the full set of trade rules in the CPTPP.

# Conclusion

Thailand’s hepatitis C treatment program in 2020 included an outdated PEG-IFN and Ribavirin regime that had more side effects and a longer treatment duration than newer, more effective DAA regimes. The DAAs included in the treatment regime were not pan-genotypic and therefore required genotype testing which added cost and complexity to the treatment program. The most expensive scenario in this study was if Thailand joined the CPTPP and the suspended clauses were reinstated, and compulsory licensing was not invoked. This was more than ten times the cost of the 2020 DAA treatment program. The cheapest scenario for Thailand is to use a generic pan-genotypic regime which is a viable option for Thailand as no DAA has been granted a patent to date. Thailand is at a critical juncture with regard to CPTPP membership. It needs to consider the broader implications of joining the CPTPP including the impact on the price of medicines if the USA re-joins and the suspended IP clauses are reinstated. If it fails to take heed of the risks that TRIPS-plus agreements pose, it threatens not only the sustainability and expansion of its hepatitis C program but all national treatment programs reliant on affordable generic medicines. Thailand needs to be free to draw on its own proven pharmaceutical capabilities to manufacture the medicines needed to sustain its treatment programs. Signing onto trade agreements that contain TRIPS-plus measures will threaten its ability to do this.

# References

1. The World Bank. The World Bank In Thailand 2021 [updated September 2020; cited 2021 26th March 2021]. Available from: <https://www.worldbank.org/en/country/thailand/overview>.

2. World Trade Organization. Frequently asked questions about TRIPS [ trade-related aspects of intellectual property rights ] in the WTO 2021 [cited 2021 23rd February 2021]. Available from: <https://www.wto.org/english/tratop_e/trips_e/tripfq_e.htm>.

3. TRIPS: Agreement on Trade-Related Aspects of Intellectual Property Rights., Annex 1C, 1869 U.N.T.S. 299, 33 I.L.M. 1197 (Apr. 15, 1994).

4. Agreement on Trade-related Aspects of Intellectual Property Rights. Section 5: patents Article 27 Patentable Subject Matter, Annex 1C (Apr. 15, 1994).

5. Vawda YA. Compulsory Licenses and Government Use: Challenges and Opportunities. Access to Medicines and Vaccines: Springer, Cham; 2022. p. 73-104.

6. World Trade Organization. TRIPS AND HEALTH: FREQUENTLY ASKED QUESTIONS. Compulsory licensing of pharmaceuticals and TRIPS 2021 [Available from: <https://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm>.

7. WTO OMC. FACT SHEET TRIPS and pharmaceutical patents September 2003 [15th Feb 2021]. Available from: <https://www.wto.org/english/tratop_e/trips_e/tripsfactsheet_pharma_e.pdf>.

8. Department of Disease Control. Ministry of Public Health. Compulsory License for Patented Medicines and Medical Devices: Lopinavir/Ritonavir. 24th January, B.E. 2550 (2007).

9. Ministry of Public Health. Compulsory License for Patented Medicines and Medical Devices: Letrozole. 4th January, B.E. 2551 (2008).

10. Ministry of Public Health. Compulsory License for Patented Medicines and Medical Devices: Docetaxel. 4th January, B.E. 2551 (2008).

11. Ministry of Public Health. Compulsory License for Patented Medicines and Medical Devices: Erlotinib. 4th January, B.E. 2551.

12. Ministry of Public Health. Compulsory License for Patented Medicines and Medical Devices: Imatinib. 4th January, B.E. 2551 (2008).

13. THAILAND Patent Act B.E. 2522 (1979) As Amended by the Patent Act (No. 2) B.E 2535 (1992) and the Patent Act (No. 3) B.E. 2542 (1999).

14. Puasiri W. Improving patent quality through pre-grant opposition in Thailand. J Int't Com L & Tech. 2013;8:219.

15. Trade Secrets Act B.E 2545 Amended by Trade Secret Act (No. 2) B. E 2558 (2015).

16. The 2007 Ministerial Regulation Regarding Trade Secrets (2007).

17. Theparat C. Another 3 months of studies, followed by CPTPP decision. The Bangkok Post 2021 6 FEB 2021.

18. Sanglee T. Will Thailand Ever Join the CPTPP? The Diplomat. November 05, 2021.

19. Gleeson D, Lexchin J, Lopert R, Kilic B. The trans Pacific partnership agreement, intellectual property and medicines: differential outcomes for developed and developing countries. Global Social Policy. 2018;18(1):7-27.

20. New W. TPP Texts Show Suspended IP Provisions: Intellectual Property Watch; 16/11/2017 [cited 2021 10th March 2021]. Available from: <https://www.ip-watch.org/2017/11/16/tpp-texts-show-suspended-ip-provisions/>.

21. Sakulbumrungsilp R, Kessomboon N, Udomaksorn K, Techakhunwut S, Kanchanaphiboon I, Vanichayakon T, et al. Health Impact Assessment of policies related to local pharmaceutical industry development towards technology readiness and access to medicines. 2020.

22. Moir HV, Palombi L. Patents and Trademarks: empirical evidence on'evergreening'from Australia. Available at SSRN 2365786. 2013.

23. Labonté R, Schram A, Ruckert A. The Trans-Pacific Partnership: Is it everything we feared for health? International Journal of Health Policy and Management. 2016;5(8):487.

24. Baker BK. Trans-Pacific partnership provisions in intellectual property, transparency, and investment chapters threaten access to medicines in the US and elsewhere. PLoS Medicine. 2016;13(3):e1001970.

25. Pusceddu P. Assessing access to medicines in preferential trade agreements: from the Trans-Pacific Partnership to the Comprehensive and Progressive Agreement for Trans-Pacific Partnership. IIC-International Review of Intellectual Property and Competition Law. 2018;49(9):1048-79.

26. Hailes O, Jones R, Menkes D, Freeman J, Monasterio E. Climate change, human health and the CPTPP. The New Zealand Medical Journal. 2018;131(1471):7-12.

27. Gleeson D, Lexchin J, Labonte R, Townsend B, Gagnon MA, Kohler J, et al. Analyzing the impact of trade and investment agreements on pharmaceutical policy: provisions, pathways and potential impacts. Global health. 2019;15(Suppl 1):78.

28. World Health Organization. Combating hepatitis B and C to reach elimination by 2030: advocacy brief. . 2016.

29. World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021: accountability for the global health sector strategies 2016–2021: actions for impact: web annex 2: data methods. 2021.

30. World Health Organization. Hepatitis C 24th June 2022 [cited 2022 11/8/2022]. Available from: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c>.

31. Mathur P, Kottilil S, Wilson E. Use of ribavirin for hepatitis C treatment in the modern direct-acting antiviral era. Journal of Clinical and Translational Hepatology. 2018;6(4):431.

32. Lucaciu LA, Dumitrascu DL. Depression and suicide ideation in chronic hepatitis C patients untreated and treated with interferon: prevalence, prevention, and treatment. Annals of gastroenterology: quarterly publication of the Hellenic Society of Gastroenterology. 2015;28(4):440.

33. Treatment Action Group. HCV Genotypes February 2017 [cited 2022 6/4/2022]. Available from: <https://www.treatmentactiongroup.org/publication/hcv-genotypes/>.

34. Senior M. Sovaldi makes blockbuster history, ignites drug pricing unrest. Nature Biotechnology. 2014;32(6):501.

35. Pollack A. Sales of Sovaldi, new Gilead hepatitis C drug, soar to $10.3 billion. New York Times. 2015;3.

36. Hill A, Khoo S, Fortunak J, Simmons B, Ford N. Minimum costs for producing hepatitis C direct-acting antivirals for use in large-scale treatment access programs in developing countries. Clinical Infectious Diseases. 2014;58(7):928-36.

37. Medicines Patent Pool. About Us [cited 2022 12/9/2022]. Available from: <https://medicinespatentpool.org/who-we-are/about-us>.

38. Medicines Patent Pool. Disease Areas [cited 2022 30/3/2022]. Available from: <https://medicinespatentpool.org/what-we-do/disease-areas#pills-VIRAL-HEPATITIS>.

39. Medicines Patent Pool. Affordable versions of hepatitis C medicine daclatasvir soon available in additional countries 16 March 2020 [cited 2022 30/3/2022]. Available from: <https://medicinespatentpool.org/news-publications-post/affordable-versions-of-hepatitis-c-medicine-daclatasvir-soon-available-in-additional-countries>.

40. MSF Access Campaign. Access to Sofosbuvir, Ledipasvir and Velpatasvir Analysis & Key Recomemendations on Gilead's Voluntary Licence March 2015 [cited 2022 30/3/2022]. Available from: <https://msfaccess.org/sites/default/files/MSF_assets/HepC/Docs/HEPC_Analystics_GileadHepCLicense_ENG_2015.pdf>.

41. MSF Access Campaign. Voluntary licenses and access to medicines. . October 2020.

42. Gower E EC, Blach S, Razavi-Shearer K, Razavi H,. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014;61:S45–S57.

43. Posuwan N VV, Chinchai T, Wasitthankasem R,Wanlapakorn N, Poovorawan Y,. 2019 Serological evidence of hepatitis A,B,and C virus infection in older adults in Khon Kaen,Thailand and the estimated rates of chronic hepatitis B and C virus infection in Thais. PeerJ. 2017;7:e7492.

44. Messina JP, Humphreys I, Flaxman A, Brown A, Cooke GS, Pybus OG, et al. Global distribution and prevalence of hepatitis C virus genotypes. Hepatology. 2015;61(1):77-87.

45. Wasitthankasem R, Vongpunsawad S, Siripon N, Suya C, Chulothok P, Chaiear K, et al. Genotypic distribution of hepatitis C virus in Thailand and Southeast Asia. PloS one. 2015;10(5):e0126764.

46. Sirinawasatien A, Techasirioangkun T. Sofosbuvir-based regimens in the treatment of patients with chronic hepatitis C virus infection: Real-world efficacy in Thailand. PLoS One. 2020;15(2):e0229517.

47. Wasitthankasem R, Pimsingh N, Treesun K, Posuwan N, Vichaiwattana P, Auphimai C, et al. Prevalence of hepatitis C virus in an endemic area of Thailand: burden assessment toward HCV elimination. The American Journal of Tropical Medicine and Hygiene. 2020;103(1):175.

48. Medspal. Medspal 2022 [cited 2022 6/4/2022]. Available from: <https://www.medspal.org/?countries%5B%5D=Thailand&disease_area%5B%5D=Hepatitis+C+(HCV)&page=1>.

49. Rattanavipapong W, Anothaisintawee T, Teerawattananon Y. Revisiting policy on chronic HCV treatment under the Thai Universal Health Coverage: An economic evaluation and budget impact analysis. PloS one. 2018;13(2):e0193112.

50. World Health Organization. Accelerating access to hepatitis C diagnostics and treatment: overcoming barriers in low-and middle-income countries: global progress report 2020. Accelerating access to hepatitis C diagnostics and treatment: overcoming barriers in low-and middle-income countries: global progress report 20202021.

51. Simmons B, Cooke GS, Miraldo M. Effect of voluntary licences for hepatitis C medicines on access to treatment: a difference-in-differences analysis. The Lancet Global Health. 2019;7(9):e1189-e96.

52. Code Blue. Minister Claims Imported Sofosbuvir Supply Enough For Malaysian Hepatitis C Patients 17 July 2020 [cited 2022 12th August 2022]. Available from: <https://codeblue.galencentre.org/2020/07/17/minister-claims-imported-sofosbuvir-supply-enough-for-malaysian-hepatitis-c-patients/>.

53. Gilead. Amended and Restated License Agreement. 2017.

54. Siraprapasiri T, Ongwangdee S, Benjarattanaporn P, Peerapatanapokin W, Sharma M. The impact of Thailand's public health response to the HIV epidemic 1984–2015: understanding the ingredients of success. Journal of virus eradication. 2016;2:7-14.

55. Make Medicines Affordable. TNP+ demands that Thailand’s Minister of Health “unlock” Hepatitis C treatment 28 Feb 2022 [updated 2022; cited 2022 30/3/2022]. Available from: <https://makemedicinesaffordable.org/tnp-demands-that-thailands-minister-of-health-unlock-hepatitis-c-treatment/>.

56. Kuanpoth J. Compulsory licences: law and practice in Thailand. Compulsory Licensing: Springer; 2015. p. 61-77.

57. Glaser M, Murphy AM. Patients versus patents: Thailand and the politics of access to pharmaceutical products. Journal of Third World Studies. 2010;27(1):215-34.

58. Islam MD, Kaplan WA, Trachtenberg D, Thrasher R, Gallagher KP, Wirtz VJ. Impacts of intellectual property provisions in trade treaties on access to medicine in low and middle income countries: a systematic review. Globalization and Health. 2019;15(1):88.

59. Kapczynski A, Sampat BN, Shadlen K. Trade agreements, patents, and drug prices: continuing the debate. Yale Law & Economics Research Paper. 2017(572).

1. The cost of ribavirin and pegylated interferon were not included in the calculations. This was because they are old, superseded medicines whose patents have expired in the vast majority of the world. The price of ribavirin and pegylated interferon would have been a constant for Scenarios 1-3 and therefore would not have changed the results in terms of how the cost of these Scenarios compare to one another. As mentioned in the Results and Discussion, it would have only impacted the comparison with Scenario 4 as this is a DAA only regime. [↑](#footnote-ref-1)
2. If Thailand chooses to make patents available for new uses only, then this scenario would not be valid as the only indication for the DAAs included in this scenario is for the treatment of hepatitis C at this time. The scenario is valid if Thailand chooses to make patents available for new methods of using a known product and or new processes of using a known product as that would result in secondary patents being granted for the DAAs in this scenario. [↑](#footnote-ref-2)
3. Some prices in this study were in Thai baht- these were converted into USD at 31.28 baht per USD – the average exchange rate for US$/Thai baht for 2020. [↑](#footnote-ref-3)