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Pharmaceutical Management Agency

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REQUEST FOR INFORMATION - HEPATITIS C TREATMENTS

PHARMAC is seeking information from suppliers of novel direct-acting antiviral agents (DAAs) for the treatment of hepatitis C.

This Request for Information (RFI) also seeks information from clinicians, hepatitis C healthcare professionals, others who provide support for people with hepatitis C, and those people who are affected by hepatitis C on the services that are provided for people with hepatitis C and the resourcing required for these services.

Examples of the classes of DAAs that PHARMAC is particularly interested in include:

- non-structural protein (NS) 3/4A protease inhibitors
- NS5A inhibitors
- NS5B nucleoside polymerase inhibitors
- NS5B non-nucleoside polymerase inhibitors.

PHARMAC welcomes information relating to other classes of agents available or in development to treat hepatitis C, including but not limited to cyclophilin inhibitors.

PHARMAC is particularly interested in receiving information in relation to those agents, including those in phase II & phase III clinical trials that do not need to be used in combination with pegylated interferon.

Information provided will help inform and assist PHARMAC in determining the most appropriate approach to assessing and making decisions about funding for novel DAAs.

If you wish to submit a response to the RFI, you must submit it to PHARMAC by email no later than **9am on 21 September 2015.**

Submissions and any questions you might have can be sent to hepc@pharmac.govt.nz.

1 Background

1.1 Purpose

This RFI seeks information to inform and assist PHARMAC in determining the most appropriate approach to assessing and making decisions about funding for novel DAAs for hepatitis C.

a. *Suppliers of DAAs*

PHARMAC wishes to gauge the level of interest from suppliers of DAAs in relation to potential future supply arrangements for DAAs, and obtain information on suppliers' range of DAAs. This information should include Medsafe-registered agents, agents that are registered overseas but not yet registered with Medsafe, and agents in development.

b. *People who treat or support those with hepatitis C or who are otherwise affected by hepatitis C*

PHARMAC also seeks input from clinicians, hepatitis C healthcare professionals, others who provide support for people with hepatitis C and those people who are affected by hepatitis C.

We are interested in information relating to the services that are available for people diagnosed with hepatitis C, how many people are accessing these services and the resourcing that is required for them (for example, but not limited to staff, capital, equipment costs). We are also interested in how these services might be affected if novel DAAs for hepatitis C were funded.

We note the estimates from Gane et al.[1] that there are currently approximately 20,000 people in New Zealand who are diagnosed with hepatitis C. In addition, there is estimated to be 30,000 people within New Zealand who are infected with the hepatitis C virus but are currently undiagnosed. PHARMAC welcomes the views of people involved in the treatment or support of people with hepatitis C on the implications of a potential increase in patient numbers on the services that they provide, both if treatment regimens remain as they currently are and if novel DAAs for hepatitis C were funded.

This information will help us to understand the wider implications and impacts that any decision that we may make will have on these services.

1.2 Outcome following close of RFI

We note that following this RFI PHARMAC would continue with its normal consideration process for funding applications it has received for hepatitis C DAAs, including analysis and ranking against other funding opportunities and funding from within the available budget.

PHARMAC could, following assessment of information received in response to this RFI, (at its discretion):

- commence negotiations with one or more specific supplier(s)
- undertake a competitive process for one or more DAAs

[1] Gane et al. Impact of improved treatment on disease burden of chronic hepatitis C in New Zealand NZMJ; 2014; 127:1407: 61- 74. Available from https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2014/vol-127-no-1407/6390

- decide not to progress the funding of novel DAAs at this time.

PHARMAC may also seek further advice before deciding upon its next steps, depending on the information received.

1.3 Current funding and PTAC advice

a. The following agents for the treatment of hepatitis C are currently listed in both the community and hospital sections of the Pharmaceutical Schedule:

Chemical	Brand (Supplier)	Subsidised in the community	Restrictions
Interferon alfa-2a	Roferon-A (Roche)	Fully subsidised	Prescriber restriction for community access.
Interferon alfa-2b	Intron-A (Merck, Sharp and Dohme)	Fully subsidised	Prescriber restriction for community access.
Pegylated interferon alfa-2a	Pegasys (Roche)	Fully subsidised	Special Authority restriction for community access. Hospital restriction for hospital access.
Ribavirin in combination with pegylated interferon alfa-2a	Pegasys RBV Combination Pack (Roche)	Fully subsidised	Special Authority restriction for community access. Hospital restriction for hospital access.
Boceprevir	Victrelis (Merck, Sharp and Dohme)	Fully subsidised	Special Authority restriction for community access. Hospital restriction for hospital access.

Full details of these agents, including details of any relevant restrictions, can be found on the Pharmaceutical Schedule at:

http://www.pharmac.govt.nz/patients/PharmaceuticalSchedule

b. PHARMAC has received funding applications from suppliers for different classes of DAAs, summarised in the table below.

Chemical	DAA	Brand (Supplier)
Sofosbuvir	Sofosbuvir is a pan-genotypic inhibitor of hepatitis C virus (HCV) NS5B RNA polymerase.	Sovaldi (Gilead Sciences)
Ledipasvir with sofosbuvir	Ledipasvir is a replication complex inhibitor that targets domain 1 of the HCV NS5A protein. Sofosbuvir is a pan-genotypic inhibitor of HCV NS5B RNA polymerase.	Harvoni (Gilead Sciences)

Paritaprevir/ritonavir, ombitasvir, dasabuvir	Paritaprevir is a HCV NS3/4A protease inhibitor. Ombitasvir is a HCV NS5A inhibitor. Dasabuvir is a HCV RNA-dependent RNA polymerase inhibitor (NS5B inhibitor).	Viekira Pak (AbbVie Ltd)
Simeprevir	Simeprevir is a HCV NS3/4A protease inhibitor.	Olysio (Janssen-Cilag Pty Ltd)

The progress of these applications can be followed, including access to minutes of advisory committee reviews where these have occurred, by typing the treatment name into PHARMAC's application tracker which can be found at:

http://www.pharmac.govt.nz/ApplicationTracker

c. The applications for sofosbuvir (Sovaldi) and ledipasvir with sofosbuvir (Harvoni) have undergone review by PHARMAC's clinical advisory committees, including review by the Pharmacology and Therapeutics Advisory Committee (PTAC). PTAC identified various subpopulations of people with hepatitis C infection and made its recommendations for funding according to these groups. The most recent review of these applications was by PTAC at its May 2015 meeting. Full minutes of the May 2015 PTAC meeting can be found on the PHARMAC website at:

http://www.pharmac.health.nz/assets/ptac-minutes-2015-05.pdf.

In summary, PTAC recommended:

Sofosbuvir

The Committee recommended that sofosbuvir should be funded with a high priority for the following subpopulations:

- HCV patients with decompensated cirrhosis (all genotypes[2])
- HCV patients pre/post liver transplant (all genotypes)
- HCV patients, genotype 1, 2 and 3, with essential mixed cryoglobulinaemia (with associated purpuric skin rash, cryoglobulinaemic glomerulonephritis and systemic vasculitis),

The Committee recommended that sofosbuvir should be funded for all other subpopulations with a low priority.

Ledipasvir with sofosbuvir

The Committee recommended that ledipasvir with sofosbuvir should be funded with a high priority for the following subpopulations:

- HCV patients with decompensated cirrhosis (all genotypes)
- HCV patients pre/post liver transplant (all genotypes)
- HCV patients with essential mixed cryoglobulinaemia (with associated purpuric skin rash, cryoglobulinaemic glomerulonephritis and systemic vasculitis).

The Committee recommended that ledipasvir with sofosbuvir should be funded for all other subpopulations of patients with chronic hepatitis C with a low priority based solely on fiscal risk.

[2] The distribution of HCV genotypes has been estimated as follows; genotype 1a at 45%, genotype 1b at 12%, genotype 2 at 7%, genotype 3 at 35% genotype 4 at 0.5%, genotype 5 at 0% and genotype 6 at 1%

d. The applications for paritaprevir/ritonavir, ombitasvir, dasabuvir (Viekira Pak) and simeprevir (Olysio) have not yet undergone review by PHARMAC's clinical advisory committees.

2 Request for information

PHARMAC seeks information in response to the questions posed in the appendices. Our questions are grouped according to the following respondent types:

- Suppliers (Appendix One).
- Clinicians, hepatitis C healthcare professionals, others who provide support for people with hepatitis C and those people who are affected by hepatitis C (Appendix Two).

3 Information requested under the Official Information Act

PHARMAC is not able to treat any part of your feedback as confidential unless you specifically request that it does. If you would like PHARMAC to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like withheld.

Feedback PHARMAC receives is subject to the Official Information Act 1982 (OIA) and any request to have information withheld will be considered in accordance with PHARMAC's obligations under the OIA.

4 Process and timeline

Provisional timeline (subject to change or extension)

a. Release of this request for information on 10 August 2015

b. Feedback due by 9am on 21 September 2015

c. Review of feedback in September/October 2015

d. Further discussion with submitter(s), if necessary, in October/November 2015

e. Evaluation and communication of next steps in November/December 2015.

5 Miscellaneous

(a) PHARMAC reserves the right:

(i) to make such adjustments to the above RFI process it considers appropriate, at any time during the process, provided that it notifies submitters affected by those changes

(ii) to seek clarification of any submission

(iii) to meet with any submitter in relation to its submission

(iv) to suspend this RFI process

(v) to terminate this RFI process at any time, by notifying submitters who made a response

(vi) to readvertise for more information.

(b) PHARMAC may consult or seek clinical advice from PTAC or its relevant sub-committee at any stage of the RFI process. PHARMAC will notify you if the clinical advice results in any changes to the terms of the RFI.

(c) You must not at any time initiate any communication with PHARMAC's directors or officers, the Ministry of Health, the Minister of Health or District Health Boards with a view to influencing the outcome of this RFI process.

(d) You must pay your own costs for preparing and submitting your submission.

(e) Submissions are submitted in reliance on your own knowledge, skill, and independent advice, and not in reliance on any representations made by PHARMAC.

(f) Your submission will be taken as acceptance of the terms contained in this RFI. PHARMAC may exclude your submission if you do not comply with any of the terms contained in this RFI.

(g) This is an RFI and not a tender. Your submission is not an offer capable of being converted into a contract for the supply of DAAs.

(h) PHARMAC is not liable in any way whatsoever for any direct or indirect loss (including loss of profit), damage or cost of any kind incurred by you or any other person in relation to this RFI.

Appendix One: Questions for suppliers

1. Contact details:
    a. company name of supplier
    b. contact person and title
    c. address
    d. phone
    e. email.

2. Details about your product(s) where the product has been brought to market, including:
    a. generic (chemical) name
    b. class of direct-acting antiviral agent (DAA)
    c. presentation; form and strength (eg tablet, 25 mg)
    d. brand name
    e. any therapies and medication which must be used in conjunction with the DAA
    f. details of indicative response rates, as measured by the rate of sustained virological response at 12 weeks post treatment (SVR12 rate) or other measure, for your product according to genotype, treatment duration, and patient group stratified by disease state and previous treatments received (for example, response in treatment naïve versus patients who have previously been treated) etc
    g. details of any subpopulations of people with hepatitis C for whom the product is contraindicated
    h. countries where the product is marketed and sold, and market share (if available)
    i. therapeutic product database report or similar (if available)
    j. disclosure of information on all known ongoing trials and patents using the product
    k. relevant consents held in New Zealand or overseas (eg registration under Section 20 of the 1981 Medicines Act, TGA approval, CE certification)
    l. if your product(s) is not currently being supplied to the New Zealand market, indicate the lead in time (in months) to get stock in to New Zealand, including the time taken to gain Medsafe registration if the particular product is not registered
    m. any other relevant product information.

3. Details of any therapies in development, including:
    a. generic (chemical) name

b. class of agent

c. presentation; form and strength (eg tablet, 25 mg)

d. brand name (if available)

e. indicative date you expect the therapy to be available for the New Zealand market

f. potential indication(s) for registration

g. any therapies and medication which must be used in conjunction with your product

h. details of indicative response rates, as measured by the rate of sustained virological response at 12 weeks post treatment (SVR12 rate) or other measure, for your product according to genotype, treatment duration, and patient group stratified by disease state and previous treatments received (for example, response in treatment naïve versus patients who have previously been treated) etc.

i. details of any subpopulations of patients with hepatitis C for whom the therapy may not be appropriate (for example, due to genotype, disease state, co-infection etc)

j. therapeutic product database report or similar (if available)

k. disclosure of information on all known ongoing trials and patents using the therapy

l. any other relevant therapy related information.

4. Indicative price per unit (excl GST) for the pharmaceutical(s) noted in your responses to 2 and 3 above based on:

    a. Supply restricted to the following patient groups:

        - HCV patients with decompensated cirrhosis (all genotypes)
        - HCV patients pre/post liver transplant (all genotypes)
        - HCV patients with essential mixed cryoglobulinaemia (with associated purpuric skin rash, cryoglobulinaemic glomerulonephritis and systemic vasculitis).

    b. Sole subsidised supply over a 5-year period restricted to the patient group identified in 4a.

    c. Supply restricted to the following patient groups:

        - HCV patients with decompensated cirrhosis (all genotypes)
        - HCV patients pre/post liver transplant (all genotypes)
        - HCV patients with essential mixed cryoglobulinaemia (with associated purpuric skin rash, cryoglobulinaemic glomerulonephritis and systemic vasculitis)
        - HCV patients with cirrhosis.

d. Sole subsidised supply over a 5-year period restricted to the patient group identified in 4c.

e. Supply restricted to the following patient groups:

- HCV patients with decompensated cirrhosis (all genotypes)
- HCV patients pre/post liver transplant (all genotypes)
- HCV patients with essential mixed cryoglobulinaemia (with associated purpuric skin rash, cryoglobulinaemic glomerulonephritis and systemic vasculitis)
- HCV patients with cirrhosis
- HCV patients with fibrosis.

f. Sole subsidised supply over a 5-year period restricted to the patient group identified in 4e.

g. Supply for the purposes of a hepatitis C eradication programme for New Zealand. This would be for the purposes of treating all New Zealanders who are infected with the hepatitis C virus. In your response please detail both the indicative price of the pharmaceutical alone and the price of the pharmaceutical, taking into account any resources that you would be willing to supply to support any proposed eradication programme.

h. Any other pricing proposals you wish PHARMAC to consider for the above identified groups, which could involve different supply periods or an alternative arrangement.

5. PHARMAC is interested in seeking information regarding innovative pricing arrangements that suppliers would be willing to consider. As such please indicate:

a. Whether you would be willing to negotiate an arrangement that is based on a price per outcome measure eg SVR12. If so, please detail an indicative price per outcome measure.

b. Whether you would be willing to agree to an arrangement that would be defined by a budget of a particular amount per year, which could be paid over a period of 5-10 years. Such an arrangement could provide unlimited access to the pharmaceutical for patients in New Zealand who are eligible for funded pharmaceuticals for a defined period of time, which could potentially be shorter than the payment period. If so, please detail an indicative total price per annum for payment over 5 years and an indicative price per annum for payment over 10 years.

c. Whether you would be willing to agree to an arrangement where there was a maximum fixed amount of money available for DAAs, with no limits on the number of DAAs that could be subsidised, and payments made to suppliers based on market share at the end of each year.

d. Any other innovative pricing proposals you wish PHARMAC to consider, which could include a combination of the above or an alternative arrangement.

6. Your proposed (or current) distribution and supply arrangements in New Zealand.

7. Your proposed (or current) educational support and training to patients and clinicians.

8. Any other matters that you consider should be taken in to account when PHARMAC is assessing and making decisions about funding for DAAs?

Appendix Two: Questions for clinicians, healthcare professionals, others who provide support for people with hepatitis C and those people who are affected by hepatitis C.

1. Contact details:

    a. name and title

    b. address

    c. phone

    d. email;

    e. organisation/s (if applicable) and your role within that/those organisation/s (as applicable).

2. What services do you currently provide, or are you aware of, for people infected with hepatitis C virus? For each service please detail the following:

    a. the name of the service

    b. what benefits does this service aim to provide for people with hepatitis C?

    c. approximately how many people use the service?

    d. what are the approximate costs associated with this/those service/s, both financially and in terms of other resources?

3. What do you think the impact would be on these services if the estimated 60% of undiagnosed chronic hepatitis C patients were identified? In particular, how would this impact the resources that the service has and the benefits that the service provides?

4. If a novel DAA was to be funded in New Zealand, what effect do you think this would have on these services in the following scenarios? In your response, please include the impact both in the short term and in the long term, any potential issues in terms of resource management, and key benefits and risks:

    a. DAAs are only provided for people with hepatitis C who have decompensated cirrhosis, or who are pre/post liver transplant or who have essential mixed cryoglobulinaemia.

    b. In addition to the group identified in 4a above, DAAs are also provided for people with hepatitis C who have cirrhosis.

    c. In addition to the group identified in 4a above, DAAs are also provided for people with hepatitis C who have cirrhosis or have fibrosis.

    d. DAAs are provided for the population of people currently diagnosed with hepatitis C (an estimated 20,000 people).

    e. All undiagnosed people are identified and diagnosed and DAAs are provided for the whole population of people estimated to have hepatitis C (an estimated 50,000 people).

5. Are you aware of any other services that are not specifically targeted for people who have hepatitis C, but whose services are affected by hepatitis C? For each service please detail the following:

    a. the name of the service

    b. what does this service provide?

    c. how is it affected by hepatitis C?

6. Are you aware of any other emerging treatments for the treatment of hepatitis C?

7. Are there any other matters that you consider should be taken in to account when PHARMAC is assessing and making decisions about funding for DAAs?