NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

9 August 2013

Approval of decisions involving boceprevir and pegylated interferon with/without ribavirin

PHARMAC is pleased to announce the approval of an agreement with Merck Sharp and Dohme (New Zealand) Limited (MSD) for the listing of boceprevir (Victrelis), and with Roche Products (New Zealand) Limited to amend the listing of pegylated interferon with/without ribavirin (Pegasys and Pegasys RBV Combination Pack). This was the subject of a consultation letter dated 19 July 2013 http://www.pharmac.health.nz/news/item/boceprevir-pegylated-interferon-and-ribavirin .

In summary, the effect of the decisions is

- boceprevir (Victrelis) will be funded, under Special Authority, from 1 September 2013 for treatment of patients living with chronic hepatitis C:
    - with IL-28 gene CT or TT allele; and
    - who have previously been treated with pegylated interferon and ribavirin who were partial responders, responder relapsers or were treated prior to 2004;
- Victrelis will be the only funded protease inhibitor for the treatment of hepatitis C in the community until 30 June 2016;
- the funded access criteria for pegylated interferon with/without ribavirin will be widened from 1 September 2013 to cover retreatment of patients living with chronic hepatitis C who have previously been treated with pegylated interferon and ribavirin who were partial responders, responder relapsers or were treated prior to 2004 in combination with boceprevir; and
- Pegasys will be the only funded brand of pegylated interferon with/without ribavirin in the community until 30 June 2017.
- The single unit packs of Pegasys 135 mcg prefilled syringe and Pegasys 180 mcg prefilled syringe will be delisted from 1 September 2013 as these products are not registered and are not supplied by Roche.
- Rule 3.3 of Section A: General Rules of the Pharmaceutical Schedule has been amended to allow pharmacy to claim wastage on boceprevir.

Details of the decisions

Boceprevir (Victrelis)

Boceprevir will be listed in Section B and Part II of Section H, of the Pharmaceutical Schedule from 1 September 2013 at the following price and subsidy (ex-manufacturer, excluding GST):

Level 9, 40 Mercer Street, PO Box 10-254, Wellington 6143, New Zealand
Phone: 64 4 460 4990 - Fax: 64 4 460 4995 - www.pharmac.govt.nz

Chemical	Presentation	Brand	Pack size	Price and subsidy
Boceprevir	Capsule	Victrelis	336	$5,015.00

- A confidential rebate will apply to all subsidised dispensings in the community (for the avoidance of doubt, the rebate will not apply to purchases by DHB hospitals).

- Victrelis will be the only protease inhibitor funded (Sole Subsidised Supply) in the community for the treatment of hepatitis C until 30 June 2016.

- Victrelis will be subject to the following restrictions in Section B and Part II of Section H from 1 September 2013:

  Initial application — (chronic hepatitis C – genotype 1, first-line) from gastroenterologist, infectious disease physician or general physician. Approvals valid for 18 months for applications meeting the following criteria:
  All of the following:
  1 Patient has chronic hepatitis C, genotype 1; and
  2 Patient has not received prior pegylated interferon treatment; and
  3 Patient has IL-28B genotype CT or TT; and
  4 Patient is to be treated in combination with pegylated interferon and ribavirin; and
  5 Patient is hepatitis C protease inhibitor treatment-naive; and
  6 Maximum of 44 weeks therapy.

  Initial application — (chronic hepatitis C – genotype 1, second-line) from gastroenterologist, infectious disease physician or general physician. Approvals valid for 18 months for applications meeting the following criteria:
  All of the following:
  1 Patient has chronic hepatitis C, genotype 1; and
  2 Patient has received pegylated interferon treatment; and
  3 Any one of:
    3.1. Patient was a responder relapser; or
    3.2. Patient was a partial responder; or
    3.3. Patient received pegylated interferon prior to 2004; and
  4 Patient is to be treated in combination with pegylated interferon and ribavirin; and
  5 Maximum of 44 weeks therapy.
  Note: Due to risk of severe sepsis boceprevir should not be initiated if either Platelet count <100 $x10^9$ /l or Albumin <35 g/l.
  Note: the wastage rule applies to boceprevir to allow dispensing to occur more frequently than monthly.

Amendment of rule 3.3 of Section A: General Rules

After considering a response to consultation requesting that boceprevir be made an OP (original pack) for the purposes of claiming, PHARMAC has amended rule 3.3 to allow pharmacy to claim wastage for this product. The intent of this change is to allow pharmacy to dispense boceprevir in frequencies less than monthly for patients who require this service (i.e., weekly dispensings) without the risk that the remainder of the pack would not be collected.

Pegylated Interferon with/without ribavirin (Pegasys and Pegasys RBV Combination Pack)

The price and subsidy for the following presentations of the Pegasys brands of pegylated interferon with/without ribavirin will be amended in Section B and listed in Part II of Section H of the Pharmaceutical Schedule from 1 September 2013 as follows (prices and subsidies expressed ex-manufacturer, excluding GST):

Chemical	Presentation	Brand	Pack size	Current price and subsidy	Price and subsidy from 1 September 2013
Pegylated interferon alfa 2a	Inj 180 mcg prefilled syringe	Pegasys	4	$1,800.00	$900.00
Pegylated interferon alfa 2a	Inj 180 mcg prefilled syringe × 4 with ribavirin tab 200 mg × 112	Pegasys RBV Combination Pack	1 OP	$2,059.84	$1,159.84
Pegylated interferon alfa 2a	Inj 180 mcg prefilled syringe × 4 with ribavirin tab 200 mg × 168	Pegasys RBV Combination Pack	1 OP	$2,190.00	$1,290.00

- A confidential rebate will apply to all subsidised dispensings in the community (for the avoidance of doubt, the rebate will not apply to purchases by DHB hospitals).

- Pegasys will be the only pegylated interferon alfa with/without ribavirin funded (Sole Subsidised Supply) in the community until 30 June 2017.

- Pegylated interferon with/without ribavirin will be subject to the following restrictions in Section B and Part II of Section H from 1 September 2013:

  Initial application — (chronic hepatitis C - genotype 1, 4, 5 or 6 infection or co-infection with HIV or genotype 2 or 3 post liver transplant) from any specialist. Approvals valid for 18 months for applications meeting the following criteria:
  Both:
  1. Any of the following:
     1.1 Patient has chronic hepatitis C, genotype 1, 4, 5 or 6 infection; or
     1.2 Patient has chronic hepatitis C and is co-infected with HIV; or
     1.3 Patient has chronic hepatitis C genotype 2 or 3 and has received a liver transplant; and
  2. Maximum of 48 weeks therapy.

  Notes:
  Consider stopping treatment if there is absence of a virological response (defined as at least a 2-log reduction in viral load) following 12 weeks of treatment since this is predictive of treatment failure.
  Consider reducing treatment to 24 weeks if serum HCV RNA level at Week 4 is undetectable by sensitive PCR assay (less than 50IU/ml) AND Baseline serum HCV RNA is less than 400,000IU/ml.

Renewal application — (Chronic hepatitis C – genotype 1 infection) from gastroenterologist, infectious disease physician or general physician. Approvals valid for 18 months for patients meeting the following criteria:
All of the following:
1. Patient has chronic hepatitis C, genotype 1; and
2. Patient has had previous treatment with pegylated interferon and ribavirin; and
3. Either:
    3.1. Patient has responder relapsed; or
    3.2. Patient was a partial responder; and
4. Patient is to be treated in combination with boceprevir; and
5. Maximum of 48 weeks therapy.

Initial application (Chronic Hepatitis C – genotype 1 infection treatment more than 4 years prior) from Gastroenterologist, infectious disease physician or general physician. Approvals valid for 18 months for patients meeting the following criteria:
All of the following
1. Patient has chronic hepatitis C, genotype 1; and
2. Patient has had previous treatment with pegylated interferon and ribavirin; and
3. Either:
    3.1. Patient has responder relapsed; or
    3.2. Patient was a partial responder; or
    3.3. Patient received interferon treatment prior to 2004; and
4. Patient is to be treated in combination with boceprevir; and
5. Maximum of 48 weeks therapy.

Initial application — (chronic hepatitis C - genotype 2 or 3 infection without co-infection with HIV) from any specialist. Approvals valid for 12 months for applications meeting the following criteria:
Both:
1. Patient has chronic hepatitis C, genotype 2 or 3 infection; and
2. Maximum of 6 months therapy.

Initial application — (Hepatitis B) only from a gastroenterologist, infectious disease specialist or general physician. Approvals valid for 18 months for applications meeting the following criteria:
All of the following:
1 Patient has confirmed Hepatitis B infection (HBsAg positive for more than 6 months); and
2 Patient is Hepatitis B treatment-naive; and
3 ALT > 2 times Upper Limit of Normal; and
4 HBV DNA < 10 log10 IU/ml; and
5 Either:
    5.1 HBeAg positive; or
    5.2 serum HBV DNA ≥ 2,000 units/ml and significant fibrosis (≥ Metavir Stage F2 or moderate fibrosis); and
6 Compensated liver disease; and
7 No continuing alcohol abuse or intravenous drug use; and
8 Not co-infected with HCV, HIV or HDV; and
9 Neither ALT nor AST > 10 times upper limit of normal; and
10 No history of hypersensitivity or contraindications to pegylated interferon; and
11 Maximum of 48 weeks therapy.

Notes:
Approved dose is 180 mcg once weekly.
The recommended dose of Pegylated Interferon alfa-2a is 180 mcg once weekly.
In patients with renal insufficiency (calculated creatinine clearance less than 50ml/min), Pegylated Interferon alfa-2a dose should be reduced to 135 mcg once weekly.

In patients with neutropaenia and thrombocytopaenia, dose should be reduced in accordance with the datasheet guidelines.
Pegylated Interferon alfa-2a is not approved for use in children.

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received by 2 August 2013 were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposal, and the following clinical issues were raised in relation to specific aspects of the proposal:

Theme	Comment
Why is there no application of a clear stopping rule for boceprevir?	The Medsafe data sheet describes response guided therapy on boceprevir. We consider that prescribers would familiarise themselves with the product before prescribing. However we intend to approach the New Zealand Society of Gastroenterology to provide information to their members on this product including appropriate treatment guidelines.
A responder queried the appropriateness of a proposal that would see only one pharmaceutical (i.e. bocepravir) in a new therapeutic group funded for a period of up to 3 years,	The Anti-Infective Subcommittee of PTAC noted that the protease inhibitors had the same or similar efficacy but differences in side effect profiles. The Subcommittee considered it would be acceptable to have only one funded protease inhibitor.
Should hepatitis C genotype 1 patients with the CC allele who have cirrhosis or advanced fibrosis have access to boceprevir in the treatment-naïve setting?	PHARMAC staff are not aware of any difference in outcomes for patients with cirrhosis and CC allele when treated with pegylated interferon and ribavirin and the Subcommittee did not consider this group required differential access. We would welcome a further submission for consideration of this patient group.
A responder noted that there are other agents on the horizon which may have less side-effects e.g. TMC435, and that the proposal would prevent entry of the new treatments for 3 years.	At this time there are only two registered protease inhibitors for hepatitis C in New Zealand. PHARMAC works within a fixed budget and must make decisions on what to fund at a point in time.
A responder requested clarification of 'partial response' in the boceprevir Special Authority	The intent was a > 2 log drop in viral load at 12 weeks. It is PHARMAC's understanding that partial response is the internationally accepted definition.
Responders asked for clarification of the status of the telaprevir proposal be following the decision to list bocepravir as the only funded protease inhibitor for the treatment of hepatitis C until 30 June 2016.	The funding application for telepravir has not been declined and remains open. However, as sole supply has been awarded to bocepravir there is no opportunity to list telaprevir for hepatitis C until after 30 June 2016. We apologise for any confusion our consultation letter might have caused around this point.
Boceprevir and pegylated interferon with ribavirin triple therapy is poorly tolerated in patients with advanced cirrhosis and can result in severe sepsis, liver decompensation and death.	We have included a note reading absolute exclusion criteria as suggested in this response.

Theme	Comment
Responders considered that there was a financial risk to pharmacies associated with inability to claim for the remainder of partially dispensed packs of bocepravir, given its high cost.	PHARMAC has included boceprevir under the wastage rule to allow the appropriate frequency of dispensing to occur without a fiscal risk to pharmacy.
Responders requested that ribavirin be available for use in hospitals for respiratory viral infections in severe immunosuppression, in particular in immunocompromised children, noting that this use would be infrequent.	PHARMAC will treat this response as a clinician application for ribavirin (oral and IV) and will assess it for funding according to its usual processes.

More information

If you have any questions about this decision, you can call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.