CONSULTATION

PHARMAC
Pharmaceutical Management Agency

4 April 2013

Proposal to amend the listing of various pharmaceuticals in the Infections group

PHARMAC is seeking feedback on a proposal to amend the restrictions applying to certain pharmaceuticals in the Infections – Agents for Systemic Use Group in Section B and Part II of Section Hof the Pharmaceutical Schedule.

As part of PHARMAC's work on developing Section H the Anti-Infective Subcommittee of PTAC recommended amending the restrictions applying to several products in the Infections - Agents for Systemic Use therapeutic group. The Subcommittee considered these pharmaceuticals at its meetings of 22 February 2012 and 1 March 2012 and 13 December 2012. The relevant minutes can be found at the following link:

http://www.pharmac.health.nz/about/committees/ptac/ptac-subcommittees#subcommittee_anti_infective_pharmaceuticals

The proposal would affect the following products or groups and apply to both Section B and Part II of Section H as applicable.

Antibacterials

- Cefazolin sodium
- Ceftriaxone sodium
- Minocycline
- Gentamicin sulphate
- Vancomycin hydrochloride
- Moxifloxacin

Antifungals

- Fluconazole

Antivirals

- Lamivudine
- Entecavir
- Valaciclovir
- Tenofovir disoproxil fumarate

Antiretrovirals

Immune modulators

- Pegylated interferon alpha-2a

Full details of the proposal can be found on the following pages.

All proposed changes would occur 1 July 2013.

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Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **Thursday, 18 April 2013** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do. If you would like us 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.

Details of the proposal

Antibacterials

Cefazolin sodium
In Section B of the Pharmaceutical Schedule the endorsement criteria for cefazolin sodium would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~):

> Only if prescribed for ~~dialysis or cystic fibrosis patient~~ **cellulitis in accordance with a DHB approved protocol** and the prescription is endorsed accordingly.

Ceftriaxone sodium
In Section B of the Pharmaceutical Schedule the endorsement criteria for ceftriaxone sodium would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~):

a) Up to 5 inj available on a PSO

b) Subsidised only if prescribed for a dialysis or cystic fibrosis patient, or the treatment of ~~confirmed ciprofloxacin resistant~~ gonorrhoea, **or the treatment of pelvic inflammatory disease,** or the treatment of suspected meningitis in patients who have a known allergy to penicillin, and the prescription or PSO is endorsed accordingly.

Minocycline hydrochloride
In Section B of the Pharmaceutical Schedule the 50 mg tablet form of minocycline hydrochloride would be fully subsidised under the following restriction:

> Special Authority for Manufacturers Price
> Initial application from any relevant practitioner. Approvals valid without further renewal unless notified where the patient has rosacea.

Gentamicin sulphate
In Section B of the Pharmaceutical Schedule the endorsement criteria applying to gentamicin sulphate would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~):

> Only if prescribed for a dialysis ~~or cystic fibrosis~~ patient ~~or for prophylaxis of endocarditis~~ **or complicated urinary tract infection**, and the prescription is endorsed accordingly.

Vancomycin hydrochloride
In Section B of the Pharmaceutical Schedule the endorsement criteria that apply to vancomycin hydrochloride would be amended as follows (additions in **bold**):

> Only if prescribed for a dialysis or cystic fibrosis patient or ~~in the treatment of pseudomembranous colitis or~~ for prophylaxis of endocarditis or for **treatment of Clostridium difficile following metronidazole failure** and the prescription is endorsed accordingly.

Moxifloxacin
In Section B of the Pharmaceutical Schedule the Special Authority criteria applying to moxifloxacin would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~) and the indications would be included in Part II of Section H:

> Initial application **- (Tuberculosis)** only from a respiratory specialist or infectious disease specialist. Approvals valid for 1 year for applications meeting the following criteria:

Either:

1 Both:

1.1 Active tuberculosis*; and

1.2 Any of the following:

1.2.1 Documented resistance to one or more first-line medications; or

1.2.2 Suspected resistance to one or more first-line medications (tuberculosis assumed to be contracted in an area with known resistance), as part of regimen containing other second-line agents; or

1.2.3 Impaired visual acuity (considered to preclude ethambutol use); or

1.2.4 Significant pre-existing liver disease or hepatotoxicity from tuberculosis medications; or

1.2.5 Significant documented intolerance and/or side effects following a reasonable trial of first-line medications; or

2 Mycobacterium avium-intracellulare complex not responding to other therapy or where such therapy is contraindicated.*

Renewal only from a respiratory specialist or infectious disease specialist. Approvals valid for 1 year where the treatment remains appropriate and the patient is benefiting from treatment.

Initial application - (Mycoplasma genitalium) from any relevant practitioner. Approvals valid for 7 days for applications meeting the following criteria:

Both:

1. **Has polymerase chain reaction (PCR) confirmed Mycoplasma genitalium*; and**
2. **has tried and failed to clear infection using azithromycin.**

Note: Indications marked with * are Unapproved Indications (refer to Section A: General Rules, Part I (Interpretations and Definitions) and Part IV (Miscellaneous Provisions) rule 4.6).

Antifungals

Fluconazole suspension

In Section B of the Pharmaceutical Schedule the Special Authority criteria applying to fluconazole oral suspension would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~):

Initial application **– (Systemic candidiasis)** from any relevant practitioner. Approvals valid for 6 weeks for applications meeting the following criteria:

Both:

1. Patient requires prophylaxis for, or treatment of systemic candidiasis; and
2. Patient is unable to swallow capsules.

Initial application – (Immunocompromised) from any relevant practitioner Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

1. **Patient is immunocompromised; and**
2. **Patient is at moderate to high risk of invasive fungal infection; and**
3. **Patient is unable to swallow capsules.**

Renewal **– (Systemic candidiasis)** from any relevant practitioner Approvals valid for 6 weeks for applications meeting the following criteria:

Both:

1. Patient requires prophylaxis for, or treatment of systemic candidiasis; and
2. Patient is unable to swallow capsules.

Renewal – (Immunocompromised) from any relevant practitioner. Approvals valid for 6 month for applications meeting the following criteria:

All of the following:

1. **Patient remains immunocompromised; and**
2. **Patient remains at moderate to high risk of invasive fungal infection; and**
3. **Patient is unable to swallow capsules.**

Antivirals

Lamivudine

In Section B of the Pharmaceutical Schedule the Special Authority criteria applying to lamivudine (tab 100 mg) would be amended as follows (additions in bold, deletions in strikethrough):

Initial application only from a gastroenterologist, infectious disease specialist, paediatrician or general physician. Approvals valid for 1 year for applications meeting the following criteria:

Any of the following:

~~1.1 All of the following:~~

~~1.1.1 HBsAg positive for more than 6 months; and~~

~~1.1.2 HBeAg positive or HBV DNA positive defined as > 100,000 copies per ml by quantitative PCR at a reference laboratory; and~~

~~1.1.3 ALT greater than twice upper limit of normal or bridging fibrosis or cirrhosis (Metavir stage 3 or 4 or equivalent) on liver histology or clinical/radiological evidence of cirrhosis; or~~

~~2~~**1** HBV DNA positive cirrhosis prior to liver transplantation; or

~~3~~**2** HBsAg positive and have had a liver, kidney, heart, lung or bone marrow transplant; or

~~4~~**3 Hepatitis B virus naïve patient who has received a liver transplant from an anti-HBc (Hepatitis B core antibody) positive donor; or**

~~4~~ Hepatitis B surface antigen (HbsAg) **positive** patient who is receiving chemotherapy for a malignancy, or high dose steroids (at least 20mg/day for at least 7 days) or who has received such treatment within the previous two months; **or**

5 Hepatitis B surface antigen positive patient who is receiving anti tumour necrosis factor treatment; **or**

6 Hepatitis B core antibody (anti-HBc) positive patient who is receiving rituximab plus high dose steroids (e.g. R-CHOP).

~~2. All of the following:~~

~~2.1. No continuing alcohol abuse or intravenous drug use; and~~

~~2.2. Not coinfected with HCV or HDV; and~~

~~2.3. Neither ALT nor AST greater than 10 times upper limit of normal; and~~

~~2.4. No history of hypersensitivity to lamivudine; and~~

2.5. ~~No previous lamivudine therapy with genotypically proven lamivudine resistance.~~

Renewal only from a gastroenterologist, infectious disease specialist, paediatrician or general physician. Approvals valid for 2 years for applications meeting the following criteria:

Either:

Renewal for patients who have maintained continuous treatment and response to lamivudine

1. All of the following:
   1.1. Have maintained continuous treatment with lamivudine; and
   1.2. Most recent test result shows continuing biochemical response (normal ALT); and
   1.3. HBV DNA < 100,000 copies per ml by quantitative PCR at a reference laboratory.

Renewal when given in combination with adefovir dipivoxil for patients with cirrhosis and resistance to lamivudine

2. All of the following
   2.1. lamivudine to be used in combination with adefovir dipivoxil; and
   2.2. patient is cirrhotic; and

   Documented resistance to lamivudine, defined as:
   2.3. patient has raised serum ALT (> 1 x ULN); and
   2.4. patient has HBV DNA greater than 100,000 copies per mL, or viral load = 10 fold over nadir; and
   2.5. detection of M204I or M204V mutation.

Renewal when given in combination with adefovir dipivoxil for patients with resistance to adefovir dipivoxil

3. All of the following
   3.1. lamivudine to be used in combination with adefovir dipivoxil; and
   Documented resistance to adefovir, defined as:
   3.2. patient has raised serum ALT (> 1 x ULN); and
   3.3. patient has HBV DNA greater than 100,000 copies per mL, or viral load = 10 fold over nadir; and
   3.4. detection of N236T or A181T/V mutation

Entecavir, lamivudine and pegylated interferon alpha-2a

In Section B of the Pharmaceutical Schedule the Special Authorities relating to entecavir, lamivudine and pegylated interferon alpha-2a would be amended to include the following (where appropriate) to account for use of Fibroscan in DHB hospitals (additions in **bold**):

"Metavir stage 3 or greater**, or moderate fibrosis**."

Tenofovir disoproxil fumarate

In Section B of the Pharmaceutical Schedule the Special Authority criteria applying to tenofovir disoproxil fumarate would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~):

Initial application - (Chronic Hepatitis B) Only from a gastroenterologist, infectious disease specialist or general physician. Approvals valid without further renewal, unless notified, for applications meeting the following criteria:

1. Both
   1.1. Patient has confirmed Hepatitis B infection (HBsAg positive for more than 6 months); and
   1.2. Any of the following
      1.2.1.All of the following
         1.2.1.1. Patient has had previous lamivudine, adefovir or entecavir therapy; and
         1.2.1.2. HBV DNA greater than 20,000 IU/mL or increased = 10 fold over nadir; and
         1.2.1.3. Any of the following:
            1.2.1.3.1. Lamivudine resistance - detection of M204I/V mutation; or
            1.2.1.3.2. Adefovir resistance - detection of A181T/V or N236T mutation; or
            1.2.1.3.3. Entecavir resistance - detection of relevant mutations including I169T, L180M T184S/A/I/L/G/C/M, S202C/G/I, M204V or M250I/V mutation; or
      1.2.2. Patient is either listed or has undergone liver transplantation for HBV; **or**
      1.2.3.Patient has decompensated cirrhosis with a Mayo score >20.

Initial application - (Pregnant**, Active hepatitis B)** only from a gastroenterologist, infectious disease physician or general physician. Approvals valid for **12 months** ~~4 months~~ for applications meeting the following criteria:

Both:

1 **Patient is HBsAg positive and pregnant; and**

~~2~~ ~~Either:~~

2~~.1~~ HBV DNA > 20,000 IU/mL and ALT > ULN; ~~or~~

~~2.2 HBV DNA > 100 million IU/mL and ALT normal~~.

Renewal - (Subsequent Pregnancy **or Breastfeeding**, **Active hepatitis B)** only from a gastroenterologist, infectious disease specialist or general physician. Approvals valid for **12 months** ~~4 months~~ for applications meeting the following criteria:

Both:

1 Patient is HBsAg positive and pregnant or breastfeeding; and

~~2~~ ~~Either:~~

2.1 HBV DNA > 20,000 IU/mL and ALT > ULN; ~~or~~
~~2.2 HBV DNA > 100 million IU/mL and ALT normal~~.

Initial application - (Pregnant, **prevention of vertical transmission)** only from a gastroenterologist, infectious disease specialist or general physician. Approvals valid for **6 months** ~~4 months~~ for applications meeting the following criteria:
Both:
1 Patient is HBsAg positive and pregnant; and
~~2 Either:~~
~~2.1 HBV DNA > 20,000 IU/mL and ALT > ULN; or~~
2.2 HBV DNA > ~~100~~ **20** million IU/mL and ALT normal.

Renewal - (Subsequent Pregnancy, **prevention of vertical transmission)** only from a gastroenterologist, infectious disease specialist or general physician. Approvals valid for **6 months** ~~4 months~~ for applications meeting the following criteria:
Both:
1 Patient is HBsAg positive and pregnant; and
~~2 Either:~~
~~2.1 HBV DNA > 20,000 IU/mL and ALT > ULN; or~~
2.2 HBV DNA > ~~100~~ **20** million IU/mL and ALT normal.

Valaciclovir

In Section B of the Pharmaceutical Schedule the Special Authority restriction for valaciclovir would be amended as follows (additions in **bold**):

Special Authority for Subsidy
Initial application — (recurrent genital herpes) from any medical practitioner. Approvals valid for 12 months where the patient has genital herpes with 2 or more breakthrough episodes in any 6 month period while treated with aciclovir 400 mg twice daily.
Renewal — (recurrent genital herpes) from any medical practitioner. Approvals valid for 12 months where the treatment remains appropriate and the patient is benefiting from treatment.
Initial application — (ophthalmic zoster) from any medical practitioner. Approvals valid without further renewal unless notified where the patient has previous history of ophthalmic zoster and the patient is at risk of vision impairment.
Initial application — (CMV prophylaxis) from any medical practitioner. Approvals valid for 3 months where the patient has undergone organ transplantation.
Initial application — (immunocompromised patients) from any medical practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:
1 Patients is immunocompromised; and
2 Patient has herpes zoster; and
3 Valaciclovir is to be given for a maximum of 7 days per course.

Antiretrovirals

In Section B of the Pharmaceutical Schedule the Special Authority criteria applying to antiretrovirals would be amended as follows (additions in **bold**, deletions in ~~strikethrough~~):

Initial application - (Confirmed HIV/AIDS) only from a named specialist. Approvals valid without further renewal unless notified for applications meeting the following criteria:
Both:
1 Confirmed HIV infection; and
2 Any of the following:

2.1 Symptomatic patient; or
2.2 Patient aged 12 months and under; or
2.3 Both:
2.3.1 Patient aged 1 to 5 years; and
2.3.2 Any of the following:
2.3.2.1 CD4 counts < 1,000 cells/mm³; or
2.3.2.2 CD4 counts < 0.25 × total lymphocyte count; or
2.3.2.3 Viral load counts > 100,000 copies per ml; or
2.4 Both:
2.4.1 Patient aged 6 years and over; and
2.4.2 CD4 counts < ~~350~~ **500** cells/mm³

Renewal - (Confirmed HIV/AIDS) only from a named specialist. Approvals valid without further renewal unless notified where the treatment remains appropriate and the patient is benefiting from treatment.

Initial application - (Prevention of maternal transmission) only from a named specialist. Approvals valid for 1 year for applications meeting the following criteria:

Either:

1 Prevention of maternal foetal transmission; or
2 Treatment of the newborn for up to eight weeks.

Initial application - (post-exposure prophylaxis following non-occupational exposure to HIV) only from a named specialist. Approvals valid for 4 weeks for applications meeting the following criteria:

Both:

1 Treatment course to be initiated within 72 hours post exposure; and
2 Any of the following:
2.1 Patient has had unprotected receptive anal intercourse with a known HIV positive person; or
2.2 Patient has shared intravenous injecting equipment with a known HIV positive person; or
2.3 Patient has had non-consensual intercourse and the clinician considers that the risk assessment indicates prophylaxis is required

Renewal - (second or subsequent post-exposure prophylaxis) only from a named specialist. Approvals valid for 4 weeks for applications meeting the following criteria:

Both:

1 Treatment course to be initiated within 72 hours post exposure; and
2 Any of the following:
2.1 Patient has had unprotected receptive anal intercourse with a known HIV positive person; or
2.2 Patient has shared intravenous injecting equipment with a known HIV positive person ;or
2.3 Patient has had non-consensual intercourse and the clinician considers that the risk assessment indicates prophylaxis is required.

Initial application - (Percutaneous exposure) only from a named specialist. Approvals valid for 6 weeks where the patient has percutaneous exposure to blood known to be HIV positive.

Immune modulators

Pegylated interferon alpha-2a

In Section B of the Pharmaceutical Schedule the Special Authority criteria for pegylated interferon alpha-2a would be amended as follows (additions in bold, deletions in strikethrough):

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:** ~~Either:~~

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; ~~and~~ **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.

Hepatitis C guidelines

In Section B of the Pharmaceutical Schedule the "Guidelines for the use of interferon in the treatment of hepatitis C:" would be amended, by removing the reference to liver biopsy under the 'criteria for treatment' section.