# Anti-Infective Subcommittee of PTAC
# Meeting held 22 February 2012

# (minutes for web publishing)

Anti-Infective Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*.

Note:

- that this document is not necessarily a complete record of the Anti-Infective Subcommittee meeting; only the relevant portions of the minutes relating to Anti-Infective Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.
- that any part of the minutes relating to hospital pharmaceuticals and the establishment of a national Preferred Medicines List (PML) will be released, in a complete publication with the original Hospital Pharmaceuticals Subcommittee minutes and final recommendations made by PTAC, once PTAC have reviewed each therapeutic group.

The Anti-Infective Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 10 & 11 May 2012, the record of which will be available in July 2012.

# 1 Clinically recommended action points

1.1 The Subcommittee **recommended** that PHARMAC:

*1.1.1* Amend the Antiretroviral Special Authority relating to CD4 count at initiation with a medium priority and for post exposure prophylaxis in non-consensual intercourse with medium priority

*1.1.2* List ivermectin under a Special Authority with a high priority

*1.1.3* Amend the restriction applying to ceftriaxone for gonnohorrea with a high priority

*1.1.4* Amend the endorsement restriction applying to ceftriaxone to include Pelvic Inflammatory Disease with a medium priority

*1.1.5* Widen access for azithromycin for Broncholitis Obliterans Syndrome with a high priority

*1.1.6* Amend the Special Authority relating to fluconazole suspension with a medium priority

*1.1.7* Widen access to itraconazole for tinea vesiclor where topical treatment has been ineffective with a medium priority

*1.1.8* Widen access to itraconazole for tinea unguium where terbenafine is not tolerated with a medium priority

*1.1.9* Widen access to valaciclovir for immunocompromised patients with shingles with a high priority

*1.1.10* List voriconazole under Special Authority for invasive fungal infection, resistant candidiasis with a high priority.

# 2 Therapeutic Group review

*Ceftriaxone*

2.1 The Subcommittee noted the tabled Environmental Science and Research (ESR) national resistance rates for gonorrhoea to ciprofloxacin. Members noted that the national resistance rate was now 29% and that this was across regions without much regional variability.

2.2 The Subcommittee considered that ceftriaxone was now the international first line agent for the treatment of gonnorrhea, and this was reflected in the New Zealand Sexual Health Society guidelines.

2.3 The Subcommittee **recommended** with a High priority that the restriction applying to ceftriaxone 500 mg injections should be amended as follows (deletion in strikethrough):

a) Subsidised only if prescribed for a dialysis or cystic fibrosis patient; or



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b) for the treatment of ~~confirmed ciprofloxacin-resistant~~ gonorrhoea; or
c) for the treatment of suspected meningitis in patients who have a known significant allergy to penicillin; and
d) the prescription or PSO is endorsed accordingly

2.4 The Subcommittee considered a request for consideration of amending the restriction applying to ceftriaxone 500 mg injections to allow treatment of Pelvic Inflammatory Disease (PID).

2.5 The Subcommittee considered that the diagnosis of PID was very difficult to make and it would be preferable to get test results prior to initiation of treatment. Members noted however that this patient group did require treatment and were generally a less compliant group and therefore empiric treatment was often preferable and clinically appropriate.

2.6 The Subcommittee noted that alongside ceftriaxone patients were required to take oral therapy and considered that doxycycline with metronidazole would be the preferred additional antibiotics for PID. Members noted that if compliance was likely to be a significant issue then potentially ceftriaxone with azithromycin was an alternative.

2.7 The Subcommittee considered that there would be up to 30,000 cases of PID a year and that 5 to 10% of these patients may require ceftriaxone for PID.

2.8 The Subcommittee **recommended** with a medium priority that the restriction applying to ceftriaxone 500 mg injections should be amended as follows (addition in Bold):

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

*Azithromycin*

2.9 The Subcommittee considered the requirements for azithromycin for Broncholitis Obliterans Syndrome (BOS) following lung transplant. The Subcommittee noted the current Special Authority relating to azithromycin for BOS prophylaxis following lung transplant and the previous minutes from PTAC (10 August 2010) and the Respiratory Subcommittee of PTAC (5 February 2010).

2.10 Members considered that only 20% of patients respond to azithromycin for BOS following lung transplant and that patients would stabilise or improve within six months of initiation of therapy. Members noted that if there was no response after 6 months of therapy then azithromycin should be stopped.

2.11 The Subcommittee considered it appropriate to include treatment of BOS following lung transplant and **recommended** with a high priority that PHARMAC widen funded access to azithromycin to include this indication with a six month approval and renewal criteria using the criteria in the Respiratory Subcommittee minutes of 5 February 2010.



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2.12 The Subcommittee considered an application for treatment of BOS following Bone Marrow Transplant (BMT).

2.13 The Subcommittee noted a tabled paper by Lam et al (Bone Marrow Transplant 2011; 46:1551-1556). The study was a randomised double-blinded placebo controlled study in patients with BOS after haematological stem cell transplant (HSCT). The treatment group received azithromycin 250 mg daily while the control group received placebo. The Subcommittee noted that there were no significant changes in respiratory system scores and Forced Expiratory Volume (FEV1) measurements between the treatment and control group following 3 months of treatment.

2.14 The Subcommittee **recommended** that the application for treatment of BOS following BGMT be declined.

*Fluconazole*

2.15 Members noted the correspondence from Dr MacFarlane regarding the current Special Authority for fluconazole suspension. Members noted Dr MacFarlane's request for an extension to the length of the fluconazole Special Authority for paediatric patients who develop invasive candidiasis early in the treatment of acute lymphoblastic leukaemia (ALL).

2.16 The Subcommittee considered that the current six week Special Authority renewal for fluconazole was appropriate for the majority of patients; however there may be a small group of patients for whom a longer Special Authority was appropriate. Members considered that paediatric patients at moderate to high risk of invasive fungal infection due to immunocompromised status would be appropriate for six monthly renewals. Members noted this would not increase patient numbers but would reduce clinician applications.

2.17 Members **recommended** amending the Special Authority relating to fluconazole suspension with a medium priority as follows (additions in Bold):

> Initial application 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 from any relevant practitioner Approvals valid for 6 month for applications meeting the following criteria:**
> **1. Patient is immunocompromised**
> **2. Patient is at moderate to high risk of invasive fungal infection**
> **3. Patient is unable to swallow capsules.**
>
> Renewal 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 from any relevant practitioner Approvals valid for 6 month for applications meeting the following criteria:**
> **1. Patient remains immunocompromised**



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

*Itraconazole*

2.18 The Subcommittee considered a request from Dr Arroll for general practice physicians to have funded access to itraconazole in patients with extensive or persistant tinea vesicolor.

2.19 The Subcommittee considered that topical therapy should remain as the first line treatment option for tinea vesicolor. Members **recommended** that PHARMAC consider fully funding econazole foaming solution for this indication.

2.20 The Subcommittee considered that oral therapy may result in less resistance than topical therapy.

2.21 The Subcommittee **recommended** that access be widened to itraconazole, with a medium priority, for the following indication:

> Funded for tinea vesicolor where topical treatment has not been successful and diagnosis has been confirmed by mycology and the prescription is endorsed.

2.22 The Subcommittee considered a request from Dr Arroll for widening of access for itracoanzole to treat tinea unguium.

2.23 Members noted that terbenafine was fully funded without restriction and was indicated for this infection. Members considered that terbenafine had less risk of interactions than itraconazole and should be considered as a first line treatment.

2.24 The Subcommittee considered that some patients may not tolerate terbinafine and that this group of patients would benefit from access to itraconazole.

2.25 The Subcommittee **recommended** that access be widened to itraconazole, with a medium priority, for the following indication

> Funded for tinea unguium where terbenafine has not been successful in eradication or the patient is intolerant to terbenafine and diagnosis has been confirmed by mycology and the prescription is endorsed.

2.26 The Subcommittee **recommended** the Specialist restriction remain on itraconazole for any further indications.

*Antiretrovirals*

2.27 The Subcommittee noted that all antiretrovirals that prescribers would wish to use were funded at this time and there were no outstanding pharmaceuticals requiring funding in this area. Members noted that a listing for the efavirenz liquid presentation would be beneficial.

2.28 The Subcommittee reiterated its previous recommendation that the initiation of antiretovirals should be when the CD4 count is < 500 cells/mm3 rather than the



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current < 350 cells//3. Members **recommended** this should be amended with a medium priority.

2.29 The Subcommittee considered a request from PHARMAC regarding non occupational prophylaxis following rape. The Subcommittee noted that ACC did not provide funding for antiretrovirals for rape victims. Members noted that the current Special Authority only provided funding for receptive anal intercourse.

2.30 The Subcommittee noted that not all rape resulted in additional mucosal trauma however this was more likely. Members noted that it was possible to get the HIV status of a source in approximately 45 minutes in an emergency situation. Members considered that there was the potential that therapy may be initiated where the risk of transmission was greater than 1 in 1,000 if appropriate criteria were not applied.

2.31 The Subcommittee **recommended** with a medium priority that the post-exposure prophylaxis following non-occupational exposure to HIV Special Authority be amended as follows (additions in bold):

> 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 Either:
> 2.1 Patient has had receptive anal intercourse with a known HIV positive person; or
> 2.2 Patient has had shared intravenous injecting equipment with a known HIV positive person.
> **2.3 Patient has had non-consensual intercourse and the clinician considers that the risk assessment indicates prophylaxis is required**
>
> Notes: Tenofovir disoproxil fumarate prescribed under endorsement for HIV/AIDS is included in the count of up to 4 subsidised antiretrovirals.
> Subsidies for a combination of up to four anti-retroviral medications. The combination of a protease inhibitor and low-dose ritonavir given as a booster (either as part of a combination product or separately) will be counted as one protease inhibitor for the purpose of accessing funding to antiretrovirals.
> 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 Either:
> 2.1 Patient has had receptive anal intercourse with a known HIV positive person; or
> 2.2 Patient has had shared intravenous injecting equipment with a known HIV positive person.
> **2.3 Patient has had non-consensual intercourse and the clinician considers that the risk assessment indicates prophylaxis is required**

2.32 The Subcommittee noted a verbal request from PHARMAC staff regarding prescribing of condoms by named prescribers for patients on antiretrovirals. The Subcommittee considered it appropriate for antiretroviral prescribers to include condoms on prescriptions of antiretrovirals to help reduce transmission and that PHARMAC should write to the named prescribers regarding this.



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*Valaciclovir*

2.33 The Subcommittee noted an application from Dr Briggs for the Special Authority to include treatment of shingles in the immunocompromised. Members noted that Auckland treatment guidelines recommended 3 to 5 days of treatment with either intra venous (iv) aciclovir or oral valaciclovir in immunocompromised patients. Members noted that valaciclovir had a higher bioavailablity than oral aciclovir. Members noted that nationally most patients received oral aciclovir and very few were likely to be admitted to hospital for iv aciclovir.

2.34 Members considered that there were approximately 20 cases per annum of shingles in HIV patients nationally and perhaps a further 200 cases of shingles in immunocompromised patients. Members considered there would be a small reduction in hospitalisations and the associated costs of i.v. aciclovir treatment. Members noted that valaciclovir was now off patent and there would possibly be price reductions into the future.

2.35 The Subcommittee **recommended** that the Special Authority relating to valaciclovir should be amended with a high priority with the following added as follows:

Application from any relevant practitioner.
1) Patient is immunocompromised; and
2) Patient has shingles; and
3) Treatment is for 7 days

# 3 Voriconazole

3.1 The Subcommittee noted the November 2010 PTAC relating to voriconazole, particularly the request for Special Authority criteria for invasive aspergillus and resistant candidiasis.

3.2 The Subcommittee considered the difficulty in community funding for invasive aspergillus revolved around possible infections rather than proven or probable cases. Members noted that the threshold for initiating treatment for invasive aspergillus would depend on the underlying disease state and how immunocompromised the patient was.

3.3 The Subcommittee noted that typically a patient would be initiated in hospital and this treatment would be required for discharge and therefore the treatment decision would be made prior to applying for the community funding.

3.4 The Subcommittee considered that a multidisciplinary team should be used to evaluate possible invasive aspergillus infections prior to initiation of treatment and recommended that this be a restriction on the PML for injectable amphotericin B and voriconazole. The Subcommittee further recommended that the multidisciplinary team include Infectious Disease physicians or Clinical Microbiologists and any other relevant consultant.



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3.5 The Subcommittee considered the previous prophylaxis treatment, if any, would be an important consideration prior to initiating voriconazole due to potential cross resistance.

3.6 The Subcommittee considered that for proven or probable invasive aspergillus a Special Authority should allow one month of treatment with a renewal as follows:

Application from Haematologist or Infectious Disease Physician
Approvals valid for one month for patients meeting the following criteria
1) Patient is immunocompormmissed
2) Patient has proven or probable invasive aspergillus infection

Renewal
Approvals valid for one month for patients meeting the following criteria
1) Patient remains immunocompormmissed
2) Patient continues to require treatment for proven or probable invasive aspergillus infection

3.7 The Subcommittee considered that for possible invasive aspergillus infection a Special Authority as follows would be appropriate

Application from Haematologist or Infectious Disease Physician
Approvals valid for one month for patients meeting the following criteria
1) Patient is immunocompormmissed
2) Patient has possible invasive aspergillus infection
3) Applicant is part of a multidisciplinary team including Infectious Disease physician

Renewal
Approvals valid for one month for patients meeting the following criteria
1) Patient remains immunocompormmissed
2) Patient continues to require treatment for possible invasive aspergillus infection

3.8 The Subcommittee considered that voriconazole should be funded for resistant candidiasis infections and other moulds, such as *Fusarium* spp. or *Scedosporium* spp.

3.9 The Subcommittee considered that the following Special Authority for resistant candidasis infections and other moulds would be appropriate

Application from Haematologist or Infectious Disease Physician
Approvals valid for one month for patients meeting the following criteria
1 Patient is immunocompormmissed, and
2 either
2.1 Patient has fluconazole resistant candidasis or
2.2 Patient has mould strain such as *Fusarium spp*. and *Scedosporium spp*
3 Applicant is part of a multidisciplinary team including Infectious Disease physician

Renewal
Approvals valid for one month for patients meeting the following criteria
1) Patient is immunocompormmissed, and
2) Either
3.1 Patient continues to require treatment for resistant candidiasis or
3.2 Patient continues to require treatment for one of the following mould strains..
Applicant is part of a multidisciplinary team including Infectious Disease physician+



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3.10 The Subcommittee endorsed PTACs high priority for listing of voriconazole for invasive aspergillus and resistant candidiasis and recommended listing for mould infection with a high priority.



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