Mahidol University
Wisdom of the Land

Treatment of Penicilliosis

Moderate-Severe Disease

- Liposomal amphotericin B, 3-5 mg/kg/day iv. for 2 weeks,
- followed by oral itraconazole, 400 mg/day for a subsequent duration of 10 weeks (AII),
- followed by secondary prophylaxis-oral itraconazole 200 mg/day for prevention of recurrence until receive combination ART and have CD4 counts >100 cells/mm^3 for ≥6 months.

Mild disease

NNRTIs can slightly decrease blood levels of itraconazole

- oral itraconazole 400 mg/day for 8 weeks (BII)

U.S. Department of Health and Human Services, 2017, at https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/349/penicilliosis

Mahidol University
Wisdom of the Land

Treatment of Penicilliosis

Alternative drug for primary treatment

- IV voriconazole, 6 mg/kg every 12 hours on day 1 and then 4 mg/kg every 12 hours for at least 3 days, followed by oral voriconazole, 200 mg twice daily for a maximum of 12 weeks.
- Patients with mild disease can be initially treated with oral voriconazole 400 mg twice a day on day 1, and then 200 mg twice daily for 12 weeks (BII).
- The optimal dose of voriconazole for secondary prophylaxis after 12 weeks has not been studied

Non HIV ????

U.S. Department of Health and Human Services, 2017, at https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/349/penicilliosis

Mahidol University
Wisdom of the Land

Table 4 Treatment outcome of penicilliosis marneffei patients with and without HIV infection

Variables	Number of patients (%)		p-values
	HIV-infected patients (N = 116)	HIV-uninfected patients (N = 34)	
Treatment received	102 (87.9)	30 (88.2)	1.000
Medication			0.823
-Amphotericin B then itraconazole	71 (69.6)	20 (66.7)	
-Itraconazole	31 (30.4)	10 (33.3)	
Outcome			0.351
-Recovery	92 (79.3)	24 (70.6)	
-Dead	24 (20.7)	10 (29.4)	
Treatment duration (days) (median, IQR)	84 (84, 90)	180 (84, 180)	<0.001

0.6-1.0 mg/kg/day for 2 weeks

8 to 10 weeks

Penicilliosis marneffei (1), mixed infection with Salmonella enteritidis (1), and hospital-acquired infections (8).

Kawila R, Chaiwarith R, Supparatpinyo K BMC Infect Dis. 2013;13:464.

Mahidol University
Wisdom of the Land

AIDSinfo

Treatment of Histoplasmosis

Moderately Severe to Severe Disseminated Disease in AIDS pt

Induction Therapy

- Preferred Therapy: Liposomal amphotericin B at 3 mg/kg IV daily (AI)
- Alternative Therapy: Amphotericin B lipid complex or amphotericin B cholesteryl sulfate complex 3 mg/kg IV daily (AIII)

Duration: For at least 2 weeks or until clinically improved

- Maintenance Therapy: Itraconazole 200 mg PO TID for 3 days, then BID for at least 12 months (AII)

[Itraconazole level >1 µg/mL, Itraconazole oral solution is preferred over capsule]

U.S. Department of Health and Human Services, 2017, at https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines

Mahidol University
Wisdom of the Land

AIDSinfo

Treatment of Histoplasmosis

Alternative Therapy in AIDS pt

Note: These recommendations are based on limited clinical data (for patients intolerant to itraconazole who are only moderately ill)

- Posaconazole 400 mg PO BID (**BIII**)
- Voriconazole 400 mg PO BID for 1 day, then 200 mg PO BID (**BIII**)
- Fluconazole 800 mg PO daily (**CII**)

U.S. Department of Health and Human Services, 2017, at https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines

Mahidol University
Wisdom of the Land

Treatment of Penicilliosis & Histoplasmosis

Disseminated disease

- Amphotericin B 0.6-0.7 mg/kg/day for 1-2 weeks,
- Oral itraconazole, 200 mg three times daily for 3 days followed by itraconazole 200 mg bid for at least 10—12 weeks
- Maintenance of itraconazole of at least 200 mg/day is recommended

Alternative Therapy

- Amphotericin B 0.4-0.5 mg/kg/day for 10-12 weeks
- Fluconazole 800 mg PO daily

แนวทางการตรวจรักษาและป้องกันการติดเชื้อเอชไอวี ประเทศไทย ปี 2560

Mahidol University
Wisdom of the Land

Prevention of endemic fungi in AIDS pt

AIDSinfo

Indication for Primary Prophylaxis

- All HIV-infected patients with CD4 counts <100 cells/mm^3 who reside or stay for a **long period in northern Thailand, Vietnam, and southern China,** and particularly in rural areas, should be administered primary prophylaxis (**BI**).
- The preferred drug for prophylaxis is **oral itraconazole, 200 mg/day** (**BI**). An alternative drug is **oral fluconazole 400 mg once weekly** (**BII**)

"A double-blind, placebo-controlled study from Chiang Mai, Thailand, demonstrated that **oral itraconazole, 200 mg daily** for primary prophylaxis, significantly reduced occurrence of systemic fungal infections (cryptococcosis and penicilliosis) in HIV-infected patients with CD4 counts <200 cells/mm^3. Fluconazole may also be effective prophylaxis"

https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/349/penicilliosis

Mahidol University
Wisdom of the Land

Prevention of endemic fungi in AIDS pt

- Primary prophylaxis สำหรับป้องกัน cryptococcosis, penicilliosis, histoplasmosis ในผู้ติดเชื้อเอชไอวีที่มีข้อบ่งชี้นั้น อาจพิจารณาให้เฉพาะใน รายที่ไม่สามารถเริ่มการรักษาด้วยยาต้านเอชไอวีได้เร็ว (optional)

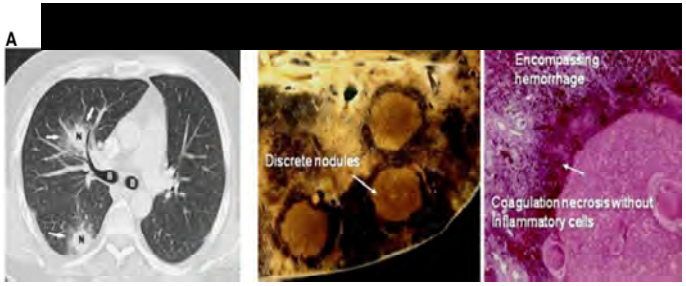
Primary prophylaxis

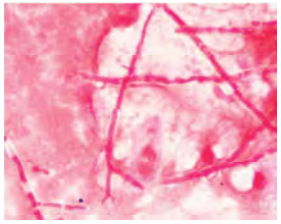
- ในผู้ใหญ่ที่มี CD4 < 100 cells/mm^3 (penicilliosis) และ 150 cells/mm^3 (histoplasmosis) ที่อยู่ในพื้นที่ที่มีเชื้อนี้ชุกชุม
- itraconazole 200 มก. กินวันละครั้ง (หากใช้ itraconazole ป้องกัน histoplasmosis หรือ penicilliosisแล้ว ไม่ต้องให้ fluconazole เพื่อป้องกัน cryptococcosis อีก)
- การหยุดให้ยาป้องกัน ผู้ที่ได้ยาต้านเอชไอวีและ CD4 > 100 cells/mm^3 (penicilliosis) และ 150 cells/mm^3 (histoplasmosis) นานกว่า 6 เดือนสามารถหยุดยาได้

แนวทางการตรวจรักษาและป้องกันการติดเชื้อเอชไอวี ประเทศไทย ปี 2560

Mahidol University
Wisdom of the Land

Invasive Aspergillosis





Georgiadou et al. CID 2011

Mahidol University
Wisdom of the Land

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

Prophylaxis-primary treatment

Posaconazole

- Oral suspension: 200 mg TID
- Tablet: 300 mg BID on day 1, then 300 mg daily
- IV: 300 mg BID on day 1, then 300 mg daily

Prophylaxis-alternative treatment

- Voriconazole (200 mg PO BID)
- Itraconazole suspension (200 mg PO every 12 h)
- Micafungin (50–100 mg/day)
- Caspofungin (50 mg/day)

Patterson et al. CID 2016

Mahidol University
Wisdom of the Land

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

Empiric therapy

- Liposomal AmB (3 mg/kg/day IV)
- Caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter)
- Micafungin (100 mg day)
- Voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h; oral therapy can be used at 200–300 mg every 12 h or 3–4 mg/kg q 12 h)

Patterson et al. CID 2016

Mahidol University
Wisdom of the Land

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

Preemptive therapy

High-risk population with evidence of invasive fungal infection (eg, pulmonary infiltrate or positive GM assay result)

- Liposomal AmB (3 mg/kg/day IV)
- Caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter)
- Micafungin (100 mg day)
- Voriconazole

Patterson et al. CID 2016