

Antifungal medications

Available antifungal medications^[1]

- Triazole antifungals: fluconazole, itraconazole, posaconazole, voriconazole.
- Imidazole antifungals: clotrimazole, econazole, miconazole, ketoconazole and tioconazole.
- Polyene antifungals: amphotericin, nystatin.
- Echinocandin antifungals: anidulafungin, caspofungin and micafungin.
- Other antifungals: these include flucytosine, griseofulvin and terbinafine and amorolfine.

NB: griseofulvin tablets are still available but have been largely superseded by other antifungal agents. It is, however, still the drug of choice in trichophyton infections in children.

Antifungal medication may be used topically or systemically. Most localised fungal infections are treated with topical preparations, but systemic treatment may be required for scalp disease, widespread infection, systemic spread, intractable infection and immunocompromised individuals.

How to use antifungal medication

Candidal vulvovaginitis^[2]

See the separate article on [Vaginal and Vulval Candidiasis](#).

- Oral fluconazole as a single dose is the first-line treatment.
- Topical imidazoles (eg, clotrimazole 1% cream) may be a useful adjunct to oral fluconazole if there are vulval symptoms.

- Intravaginal imidazole drugs (clotrimazole, econazole, fenticonazole, and miconazole) can be used if fluconazole is contra-indicated or not tolerated.
- Imidazole drugs (clotrimazole, econazole, fenticonazole, and miconazole) are effective in the treatment of vulvovaginal candidiasis. Oral treatment with fluconazole or itraconazole is also effective.
- Oral antifungal treatment should be avoided during pregnancy; intravaginal clotrimazole is preferred in this situation.
- In recurrent vulvovaginal candidiasis, an induction-and-maintenance regime may be used: three doses of oral fluconazole 150 mg taken every three days, and then one dose of oral fluconazole taken every week for up to six months.
- For severe candidal vulvovaginitis, treatment should be repeated at 72 hours; ie fluconazole 150 mg orally on day 1 and day 4, or clotrimazole 500 mg pessaries on day 1 and day 4.

In immunocompromised individuals, oral antifungals for seven days, or intravaginal preparations for 6-14 days are advised.

Oral candidiasis^[3]

See the separate article on [Candidiasis](#).

- First-line therapy is with topical treatment with miconazole gel.
- Nystatin suspension is second-line treatment.
- For extensive or severe candidiasis, prescribe oral fluconazole 50 mg a day for 14 days.
- In people with HIV and oral candidiasis, prescribe oral fluconazole 200 mg on day one, and oral fluconazole 100-200 mg daily for 14 days.
- Children should only receive topical anticandidal treatment. Offer miconazole oral gel first-line (off-label use in children less than 4 months of age). Offer nystatin suspension (off-label use in neonates) if miconazole oral gel is unsuitable.

Nail infections^[4]

See the separate article on [Fungal Nail Infections](#).

- For mild infections use topical amorolfine nail lacquer first-line. Use for six months for fingernails and 9-12 months for toenails.
- Oral terbinafine is the first-line oral treatment. Treat for between six weeks and three months for fingernails and for between three and six months for toenails.
- Oral terbinafine can cause drug-induced liver injury, and requires monitoring of liver function tests during therapy. However, this risk is relatively small - with an estimated probability of developing elevated serum aminotransferase levels requiring stopping treatment of 0.44% for treatment longer than eight weeks, and clinically apparent liver injury from terbinafine occurring rarely (between 1 in 50,000 to 1 in 120,000 prescriptions).^[5]
- Oral itraconazole is an alternative. (Terbinafine is most effective against dermatophyte nail infections. It has fungistatic activity against *Candida albicans*. Itraconazole is highly active against *Candida* spp. but much less so against dermatophytes.) Prescribe itraconazole as pulsed therapy, 200 mg twice a day for a week, repeating the course after 21 days. Two pulses should be used for fingernails, and three for toenails.
- Griseofulvin can be considered if both terbinafine and itraconazole are contra-indicated.

Skin infections^[6]

See the separate articles on [Candidiasis](#), [Tinea Capitis](#), [Pityriasis Versicolor](#) and [Dermatophytosis \(Tinea Infections\)](#).

- Topical antifungals should be prescribed in most cases. Terbinafine and the imidazoles (clotrimazole, econazole, and miconazole) are all effective.
- Systemic treatment is only indicated in severe, extensive skin infection, or if there is associated systemic infection (eg, in immunosuppressed people), or in the rare person unresponsive to topical treatment.

- Oral treatment is recommended first-line for tinea capitis.^[7] This would be griseofulvin or terbinafine (off-label.) Microbiological sampling should be performed prior to starting treatment, to guide antifungal choice later. A topical shampoo can be used alongside oral antifungals, for the first two to four weeks of oral treatment, to reduce the risk of transmission to others. Imidazole creams for one week are another option. If the diagnosis is certain and there is appropriate expertise and experience available, treatment can be initiated in primary care; otherwise, specialist advice should be sought.

Fungal ear infections

See the separate article on [Fungal Ear Infection \(Otomycosis\)](#).

Fungal eye infections

Most fungi causing orbital infections are ubiquitous aerobic organisms that are normal commensals of the respiratory, gastrointestinal and female genital tracts, as well as sometimes being present on normal conjunctiva.

Fungal eye infections are rare in Western countries; they are more frequently seen in tropical and subtropical regions.

Fungal infections of the eye may cause orbital cellulitis, dacryocystitis, conjunctivitis, keratitis and endophthalmitis.^[8] Thus, they can work at a superficial level or penetrate deeply into the eye.^[9]

Antifungal medication treatment is initiated and monitored by a specialist ophthalmology team. Samples such as corneal scrapes will have been obtained prior to initiation of therapy. Any steroid treatment needs to be discontinued. Antifungal preparations for the eye are not generally available and have to be specifically made up under specialist direction for each patient.^[1]

Systemic fungal infections

See also the separate articles on [Aspergillosis](#), [Candidiasis](#), [Cryptococcosis](#), [Fungal Lung Infections](#) and [Systemic Mycoses](#).

Specialist treatment is required in most forms of systemic or disseminated fungal infections.

Immunocompromised patients^[1]

Immunocompromised patients are at increased risk of fungal infections and may need prophylactic antifungal drugs. Management is a challenge, and a specialist field, and guidelines differ.^[10]

Oral triazole antifungals are the drugs of choice for prophylaxis. Fluconazole is more reliably absorbed than itraconazole but is not effective against *Aspergillus* spp. Therefore, itraconazole is preferred in patients at risk of invasive aspergillosis. (Voriconazole is the treatment of choice for established aspergillosis.)

Posaconazole can be used for prophylaxis in patients who are undergoing haematopoietic stem cell transplantation or receiving chemotherapy for acute myeloid leukaemia and myelodysplastic syndrome, particularly if the incidence of invasive mould diseases is high.^[11] Micafungin can be used when fluconazole, itraconazole or posaconazole cannot be used.

Amphotericin by intravenous infusion or caspofungin is used for the empirical treatment of serious fungal infections. Caspofungin is not effective against fungal infections of the central nervous system.

Cautions and contra-indications^[1]

Important information

Amphotericin has a risk of toxicity when given parenterally. It should only be used parenterally in hospitalised patients, or for those under close clinical observation. It should be avoided if possible in those with renal impairment, and in pregnant women. A test dose is required. After this, the patient is observed closely for 30 minutes. Rapid infusion carries a risk of arrhythmias. Close monitoring is required of renal function, hepatic function, blood count, as well as potassium and magnesium levels.

Fluconazole carries a risk of hepatic impairment. Use with caution in pregnancy, breast-feeding and impaired liver function. It is **CONTRA-INDICATED** in acute porphyria.

Oral ketoconazole (for any indication) is not recommended, as the risks outweigh the benefits.^[12]

Griseofulvin may impair the ability to perform skilled tasks - eg, driving. The toxic effects of alcohol are increased. It is **CONTRA-INDICATED** in severe liver disease, acute porphyria and systemic lupus erythematosus (SLE). Avoid in pregnancy and hepatic impairment.

Miconazole gel is **CONTRA-INDICATED** in infants with an impaired swallowing reflex, and in the first six months of life for preterm infants. Avoid in liver disease, pregnancy, breast-feeding and acute porphyria.

Oral terbinafine should be used with caution in liver or kidney disease, psoriasis (may exacerbate), autoimmune disease, pregnancy or breast-feeding. Liver function should be checked before starting treatment, and monitored every four to six weeks.

NB: many nystatin preparations are now withdrawn. This includes vaginal cream, pessaries, pastilles and Tri-Adcortyl Otic®.

Adverse effects^[1]

Many antifungal medications have similar adverse effects. They all may cause gastrointestinal upset, rashes, headaches, etc. In addition:

- Amphotericin may cause muscle and joint pain, hypokalaemia/hypomagnesaemia, hearing loss, diplopia, convulsions or peripheral neuropathy.

- Fluconazole may cause LFT abnormalities, and rash – [toxic epidermal necrolysis](#) and [Stevens–Johnson syndrome](#) have been reported.
- Griseofulvin may aggravate or precipitate [systemic lupus erythematosus \(SLE\)](#).
- Flucytosine may cause marrow aplasia.
- Application of topical imidazoles can be painful in some instances where there is particularly bad inflammation.
- Terbinafine is associated with loss of taste.

Further reading

- [Fungal skin infections](#); DermNet NZ
- [Fungal Skin and Nail Infections: Diagnosis and Laboratory Investigation – Quick Reference Guide for Primary Care](#); GOV.UK, 2017

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