

# Griseofulvin

Griseofulvin is an oral antifungal medication used primarily in the treatment of various dermatophyte infections, including tinea (ringworm) and onychomycosis (fungal nail infections). Initially isolated from the *Penicillium* species in 1939, griseofulvin was originally developed as a veterinary treatment for cattle with ringworm. The drug was approved by the U.S. Food and Drug Administration in 1959 for human use. Today, griseofulvin is available in several oral formulations, including microsize and ultramicrosize, which are used to improve absorption and enhance treatment outcomes. The drug is metabolized in the liver and excreted in the urine, feces, and perspiration.

## Mechanism of Action

Griseofulvin exerts its antifungal effects through a unique mechanism of action. It is primarily fungistatic, meaning it inhibits the growth and replication of fungi rather than killing them outright. Griseofulvin acts by binding to microtubules within the fungal cell, disrupting the mitotic spindle during cell division. This disruption arrests the cell cycle at metaphase, preventing further fungal proliferation. Griseofulvin also accumulates in keratin precursor cells found in the skin, hair, nails, and other keratinized tissues, creating a localized environment that inhibits fungal growth. This mechanism makes griseofulvin especially effective for treating superficial dermatophyte infections, as it targets the keratinized layers of the skin, hair, and nails where these fungi tend to reside.

## Clinical Indications

Griseofulvin is indicated for the treatment of dermatophytosis, a group of fungal infections caused by dermatophytes, including *Trichophyton*, *Epidermophyton*, and *Microsporum* species. These infections are typically localized to the skin, nails, and hair. Griseofulvin is most commonly used in the following dermatologic conditions:

- ***Tinea barbae***: Fungal infection of the beard and mustache area.
- ***Tinea pedis***: Athlete's foot, a common fungal infection of the feet.
- ***Tinea corporis***: Ringworm affecting the body.
- ***Tinea capitis***: Fungal infection of the scalp, commonly affecting children.
- ***Tinea cruris***: Fungal infection of the groin area, also known as "jock itch."
- ***Tinea unguium (onychomycosis)***: Fungal infection of the nails, which may require prolonged therapy.

Griseofulvin is particularly effective for superficial dermatophyte infections that affect keratinized tissues, as it selectively targets keratinocytes, preventing fungal organisms from invading deeper tissues.

### Side Effects and Contraindications

While griseofulvin is generally well tolerated, it can cause a range of adverse effects. The most common side effects include:

- Rash and urticaria (hives).
- Gastrointestinal symptoms such as nausea, vomiting, and diarrhea.
- Headache, dizziness, fatigue, and insomnia.
- Photosensitivity, leading to an increased risk of sunburn.
- Hematologic effects, including leukopenia (low white blood cells).
- Renal effects, including proteinuria (protein in urine).
- Oral candidiasis and gastrointestinal bleeding in rare instances.

Griseofulvin is contraindicated in several conditions due to potential adverse effects:

- **Hypersensitivity:** Patients allergic to carbapenems, penicillin, or cephalosporins should avoid griseofulvin.
- **Liver Disease:** Griseofulvin is metabolized in the liver, and its use is contraindicated in individuals with hepatic failure or porphyria due to the risk of exacerbating liver dysfunction.
- **Pregnancy and Lactation:** Griseofulvin is classified as a Category X drug in pregnancy, meaning it should be avoided due to potential teratogenic effects. The safety of griseofulvin during lactation has not been established, and it is advised that it be avoided during breastfeeding.

### Drug Interactions

Griseofulvin has several significant drug interactions that may either reduce the effectiveness of other medications or enhance adverse effects:

- **Warfarin:** Griseofulvin can decrease the anticoagulant effect of warfarin, necessitating close monitoring of coagulation parameters during co-administration.
- **Oral Contraceptives:** Griseofulvin can reduce the efficacy of oral contraceptives, increasing the risk of unintended pregnancies.
- **Cyclosporine:** There is evidence that griseofulvin may alter cyclosporine levels, which could impact immunosuppressive therapy in organ transplant patients.

### Precautions and Monitoring

Given its hepatic metabolism, griseofulvin should be used cautiously in patients with liver dysfunction. Hematologic, liver, and renal functions should be carefully monitored during

treatment. Regular follow-up visits may be necessary to assess for side effects and to ensure the efficacy of treatment.

### **Recent Advances and Alternatives**

Although griseofulvin remains a staple in the treatment of dermatophyte infections, newer antifungal agents have emerged with potentially fewer side effects and more convenient dosing regimens. Terbinafine, an allylamine antifungal, is now often preferred for the treatment of onychomycosis due to its shorter treatment duration and superior efficacy compared to griseofulvin. Itraconazole and fluconazole are also alternative treatments for dermatophyte infections, particularly when systemic therapy is required.

However, griseofulvin remains a valuable option, particularly in pediatric patients or cases where other therapies are contraindicated or poorly tolerated. Its efficacy in treating tinea infections of the scalp and nails, where long-term treatment may be necessary, continues to be well documented.

### **Conclusion**

Griseofulvin is an effective oral antifungal used in the treatment of dermatophyte infections, including tinea and onychomycosis. Its mechanism of action, which disrupts mitotic spindle formation and selectively targets keratinized tissues, makes it well-suited for superficial fungal infections. While it is generally well tolerated, potential side effects such as gastrointestinal symptoms, photosensitivity, and liver dysfunction require monitoring. Given its interactions with other medications, careful management and patient education are essential. As newer antifungal agents offer alternative treatment options, griseofulvin remains a viable and important tool in the management of dermatophytosis.

### **References**

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