Agansit cell wall Polyenes/macrocyclic lactone

Nyastatin/Mycostatin	Amphotericin B
No oral absorptiob/toxicity.	**broadest spectrum** of all antifungals.
Uses: GIT candidiasis. DOC for vaginal or cutaneous candidiais.	Uses: DOC for deep fungal infection
	SE/toxicity: Phlebitis, nephrotoxicity.

MOA: integrate within cell wall ergosterols, causing leakage of small molecules.
Have higher affinity to fungal ergosterols than mammalian sterols.

Against fungal nucleus

Griseofulvin	5-fluorocytosine (Flucytosine)
Natural. Oral intake since topically inactive.	Synthetic pyrimidine analogue.
MOA: stops mitosis/M-phase	MOA: get incorporated into RNA, thus ruining protein synthesis.
SAR: Has 2 stereocenters(Cl and C-O-CH3)	Prodrug activated by **fungal cytosine deaminase**
-Cl can be replaced by fluorine only.	

-**Increased activity**: if Methoxy becomes propoxy or butoxy *invitro* due to increased lipophilicity. - **Decreased activity:** if methoxy becomes NH2.

Uses: agansit mycelial fungi only; fungistatic for growing dermatophytes (ringworm,tinea)	Uses: systemic fungal and candida infections.

Affecting ergosterol biosynthesis

Thiocarbamates	Allylamine deriv.		Azole deriv.	
MOA: inhibit squalene epoxidase.	MOA: inhibit squalene epoxidase.	Imidazole "1st gen."	Imidazoles "2nd gen."	Triazoles
Tolnaftate	Terbinafine, Lamisil	Clotrimazole, Miconazole	Ketoconazole	1) Fluconazole

Affecting ergosterol biosynthesis (cont)

Uses: topical for dermatophytes, Tinea cure, for skin mycoses such as athletes foot.	Oral & topically active.	Broad-spectrum with no problems topically but **systemically may cause hepatotoxicity.**	**Improved systemic bioavail.** by improving water solubility.	Use: for vaginal candidiasis.
Not very effective for nail & scalp mycoses.	Uses: for ring worm and nail infections "onychomycoses"	Miconazole is used for oral candidiasis.	The structure includes a dioxolane ring (ketal structure) responsible for the improved water solubility.	only 2,4-di-fluro variants were active and non-toxic.
		Ticoconazole		2) Itraconazole
		x4 more potent than miconazole.		Synthetic dioxolane triazole
		AB also to some G+ve bacteria (like metronidazole).		Uses: oropharyngeal or vaginal candidiasis. **Aspergillosis candidiasis.**