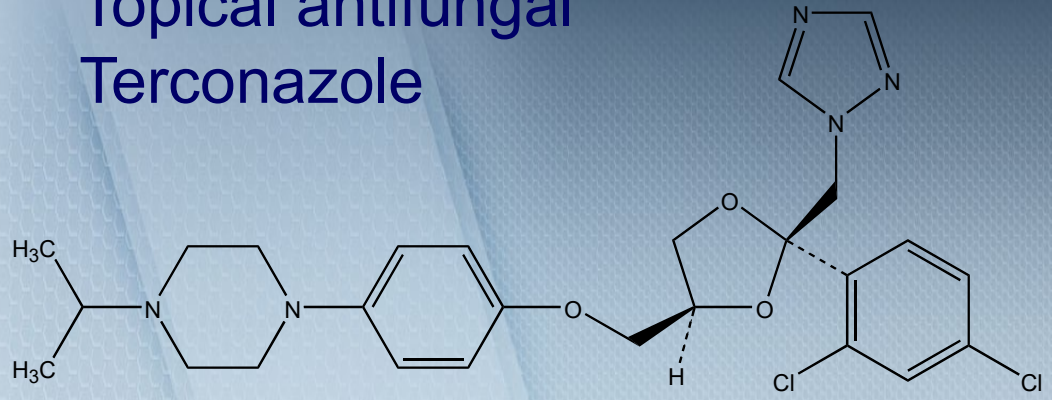
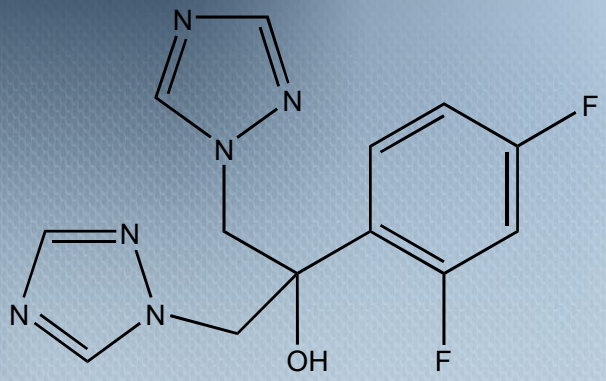
Triazole Antifungals

- The azole antifungal agents inhibit the synthesis of ergosterol by blocking the action of
- 14-alpha-demethylase.
    1. **Fluconazole**
    2. **Itraconazole**
    3. **Ketoconazole -**
    4. **Ravuconazole**
    5. **Posaconazole**
    6. **Voriconazole**
    7. **Terconazole (Topical antifungal)**

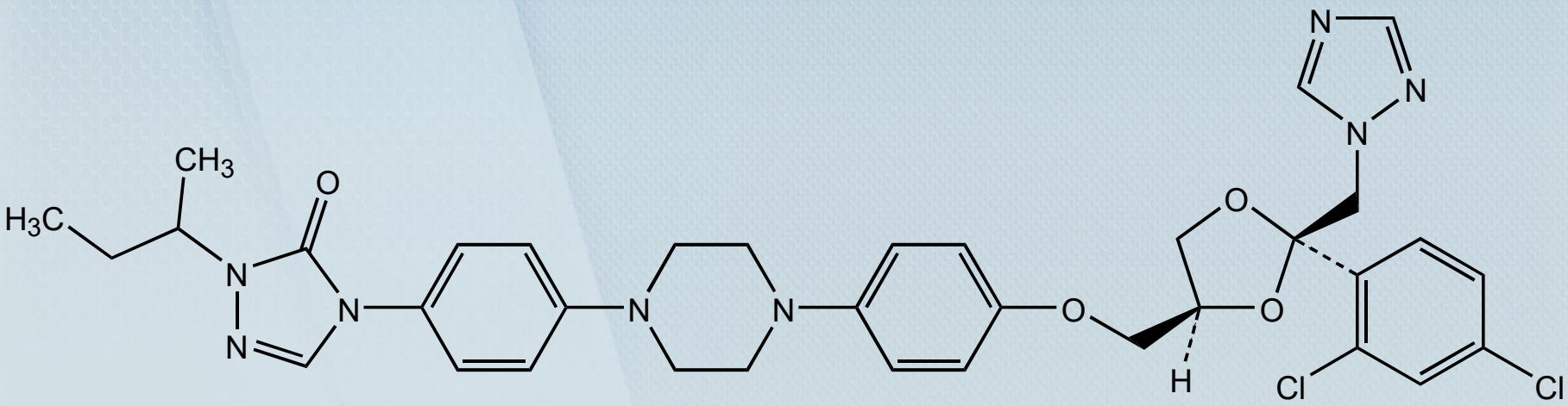
Topical antifungal

Terconazole

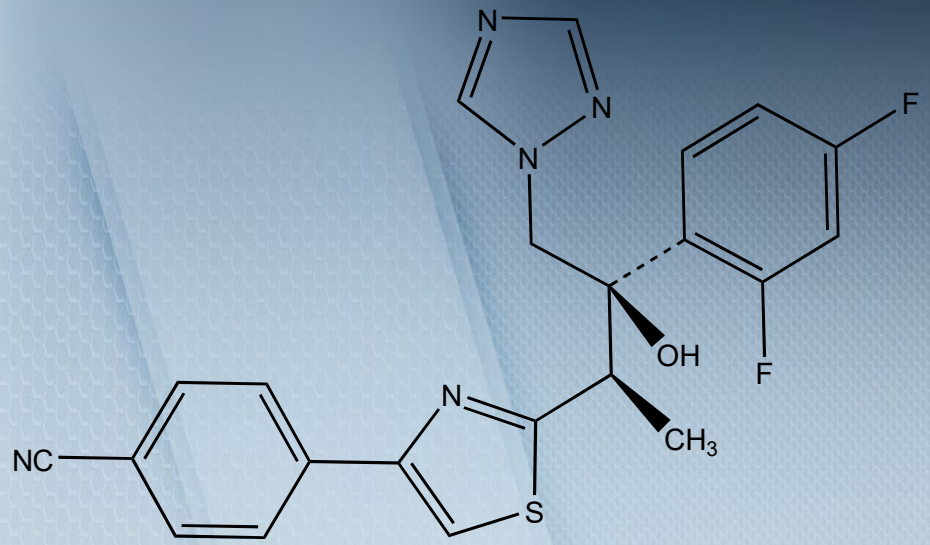




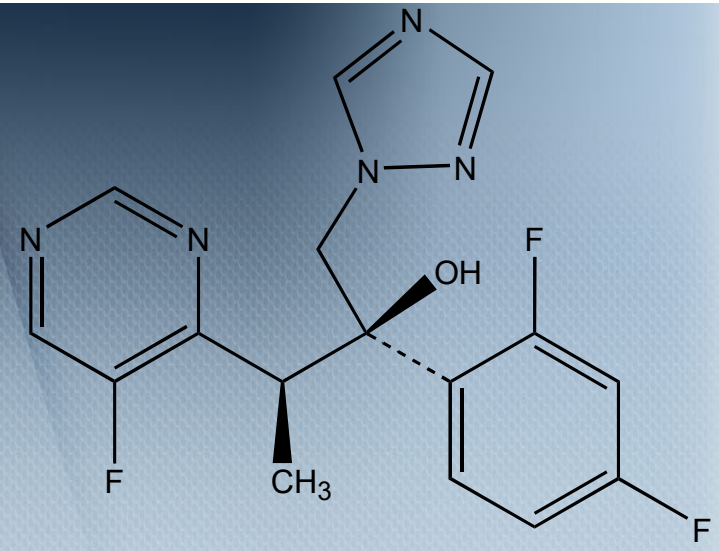
Fluconazole



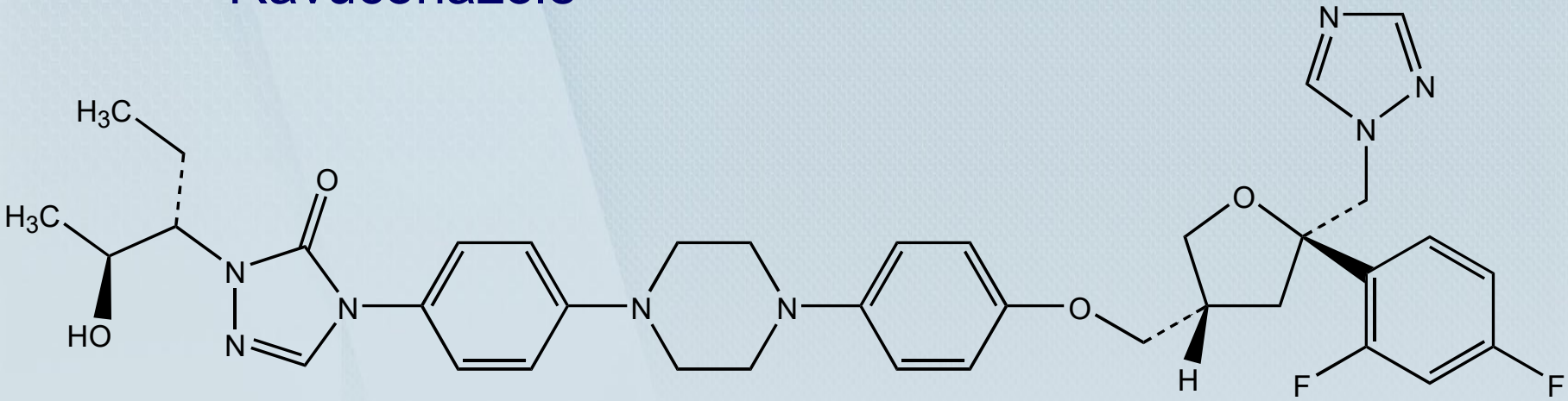
Itraconazole



Ravuconazole



Voriconazole

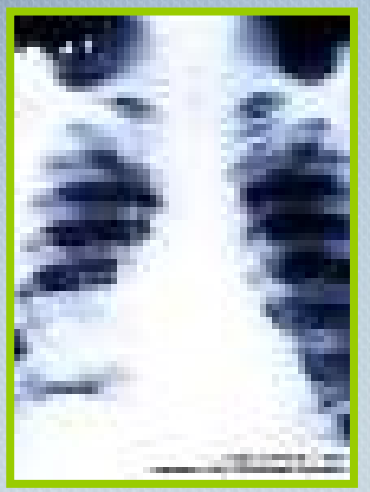


Posaconazole

Fungal infection challenge No 1 in public health

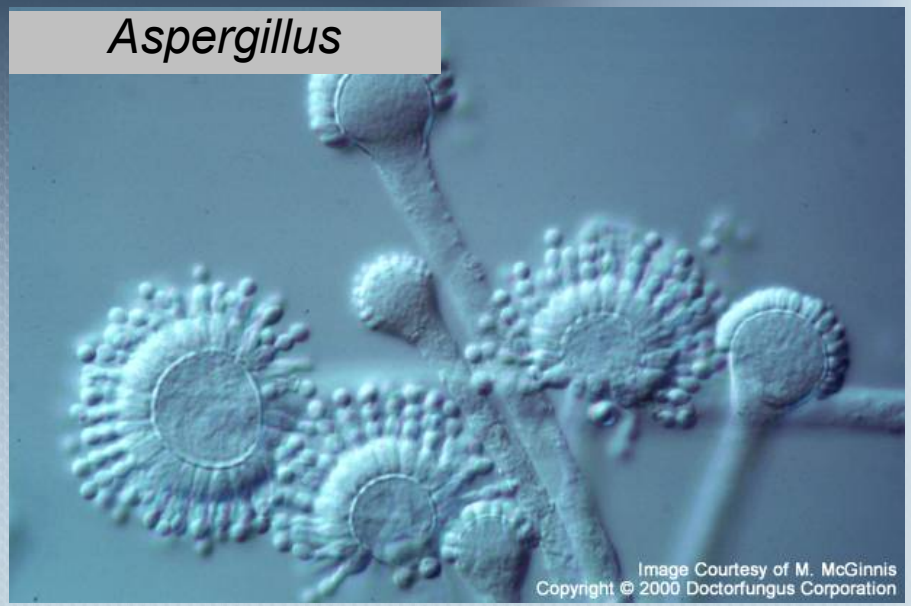
- The burden on health care of fungal infections are enormous.
- Fungal infections are common in diabetic patients, after anticancer chemotherapy, in HIV/AIDS patients.
- Resistance occurs against existing antifungal medications.
- Another important factor is effectiveness.
- Treatment of fungal infections last for several months and sometimes ineffectively and with dismal outcome, e.g. in diabetes mellitus ultimately resulting in invalidity or even death.

Fungal infections affecting multiply organs



Candida

Aspergillus



Scedosporium

Fusarium

Making New Chemical Entity Druglike

- a pharmacologically active lead structure is optimized step-wise for increased activity and selectivity, as well as drug-like properties as described by Lipinski's rule.
- A traditional method to evaluate druglikeness is to check compliance of Lipinski's Rule of Five, which covers the numbers of hydrophilic groups, molecular weight and hydrophobicity.
- Theoretically, a drug-like molecule has a logarithm of partition coefficient (log P) between -0.4 and 5.6, molecular weight 160-480 g/mol, molar refractivity of 40-130, which is related to the volume and molecular weight of the molecule and has 20-70 atoms.

Lipinski's Rule of Five

- The rule describes molecular properties important for a drug's pharmacokinetics in the human body, including their absorption, distribution, metabolism, and excretion ("ADME"). However, the rule does not predict if a compound is pharmacologically active.

- New chemical entity should satisfy such requirements as to be more safe and more effective then existing drugs.