7 days of fluconazole

Day 1: 7 days of [#fluconazole](https://twitter.com/search?q=%23fluconazole). The search for an oral + i.v active anti-fungal drug led to the discovery of [#fluconazole](https://twitter.com/search?q=%23fluconazole) in 1969. Multiple modifications to the imidazole ketoconazole gave rise to this broad spectrum triazole drug, with the desired combination of potency & polarity



Day 1 [#fluconazole](https://twitter.com/search?q=%23fluconazole) (cont): Main indications are vaginal/vulvovaginal, mucosal & dermal candidiasis, as well as tinea pedis/cruris/corporis. Candidal balanitis, treatment of invasive candidal & cryptococcal infections & prevention of immune-compromise related candidiasis

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Day 2: Kinetics [#fluconazole](https://twitter.com/search?q=%23fluconazole). Good oral bioavailability & moderate volume of distirbution. Good penetration into body fluids + high concentration to skin & nail. Minor hepatic metabolism, but 80% is excreted unchanged/hence used candiduria. NOTE: reduce dose in renal impairment if multiple dosing regimen). T½ 30-50 hrs

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Day 3; Single dose therapy of 150mg is effective as #fluconazole has a very long half-life Also used in 6-month regimen every 3 days, then weekly for recurrent vaginal candidiasis. Other infections oral dosing 50-400mg/day (higher end doses for prevention). Child i.v doses depend on age & weight

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Day 4: mechanism of action [#fluconazole](https://twitter.com/search?q=%23fluconazole); there is selective toxicity targeting ergosterol, the fungal cell membrane equivalent to cholesterol. Inhibition of the CYP450 enzyme converting lanosterol to ergosterol (lanosterol 14-α-demethylase) damages membrane function and leads to cell death

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Day 5: Adverse drug events [#fluconazole](https://twitter.com/search?q=%23fluconazole). Common: includes headache, GI disturbance, liver function test changes, skin reactions Uncommon/severe includes: seizures, myalgia, SJS, DRESS, agranulocytosis, Torsades de pointes, hepatitis (not exhaustive). High doses/extended courses can cause hepatotoxicity - monitor

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Day 6: Drug-drug interactions [#fluconazole](https://twitter.com/search?q=%23fluconazole): QT prolongation risk/ increased cardiotoxicity risk with erythromycin, citalopram, anti-arrhythmics, rifampicin. NOTE fluconazole inhibits human CYP2C19+3A4 lead to ‘severe’ DDIs with warfarin, phenytoin, tacrolimus (not exhaustive)



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Day 7:There is rising global candidal resistance to [#fluconazole](https://twitter.com/search?q=%23fluconazole), possibly because of increased long-term use e.g for immune suppression protection. Many proposed mechanisms for resistance, including increased expression of fungal efflux pumps, alteration of target proteins & alteration of membrane sterol composition

CPD: in addition to the tweets, read the BNF section on Fungal Infection ‘Antifungals,systemic use’, as well as the monograph on fluconazole. Another useful source is the Summary of Product Characteristics for fluconazole – see links below

<https://bnf.nice.org.uk/drug/fluconazole.html>

<https://www.medicines.org.uk/emc/medicine/25882#PRODUCTINFO>

CPD questions (most but not all answers will be in the tweets). There is only one correct answer per question

1. Fluconazole is effective as a single dose therapy because it has a short half-life

TRUE or FALSE

1. There is no resistance to triazole anti-fungal drugs such as fluconazole

TRUE or FALSE

1. Which is a common ADR for fluconazole?
2. SJS
3. Seizure
4. Skin reactions
5. Dry mouth
6. What is the reason why hepatic drug metabolism can be affected by fluconazole?
7. It causes liver dysfunction which lowers CYP450 levels
8. Extensive metabolism diverts CYP450 enzymes to breaking down the fluconazole
9. Its demethylation metabolism is via a CYP enzyme common to fungal and human systems and this can inhibit human CYP450 liver function
10. Fluconazole depletes CYP450 levels in the liver
11. The majority of fluconazole is excreted unchanged allowing high concentrations to treat candidal urinary tract infection caused by candida

TRUE or FALSE

1. Which of the following is TRUE?
2. Fungal cell membranes contain cholesterol
3. Child i.v doses depend on age & weight
4. Fluconazole is used to treat tinea pedis
5. Fluconazole is licensed to treat tinea capitus in children
6. Fluconazole can cause liver damage and taking other drugs which can be hepatotoxic is to be avoided

TRUE or FALSE

1. Fluconazole may be used to both prevent and treat candida infections

TRUE or FALSE

1. Which of the following is TRUE?
2. Salbutamol is predicted to cause hyponatraemia if used with fluconazole
3. The drug interaction with clarithromycin is classified as mild
4. Fluconazole increases the risk of clopidogrel related bleeding
5. Fluconazole is linked to QT prolongation
6. Fluconazole works by preventing fungal cell replication

TRUE or FALSE