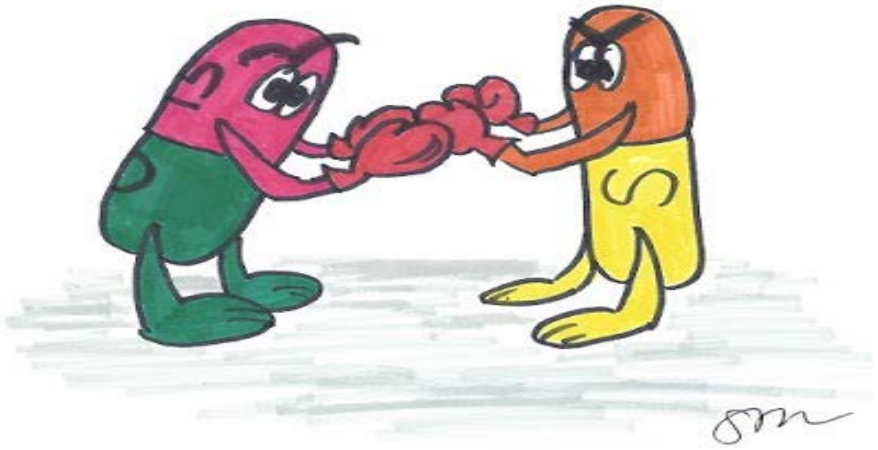
Understanding Drug Interactions for Prescribing Practice



ESNEFT/ GP Suffolk Fed –NMP Summit July 2022

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Activities

Visual settings

Edit

Respond at **PollEv.com/temia636**

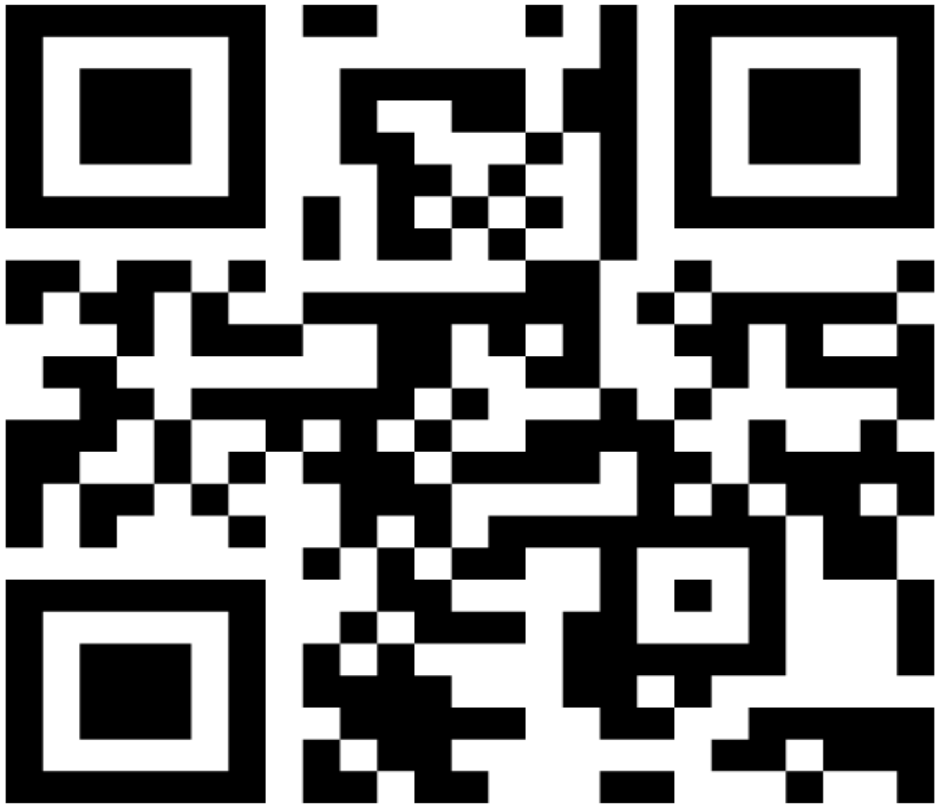
What should be monitored in a patient taking Digoxin and Bendroflumethiazide and why?

Powered by Poll Everywhere

Session objectives

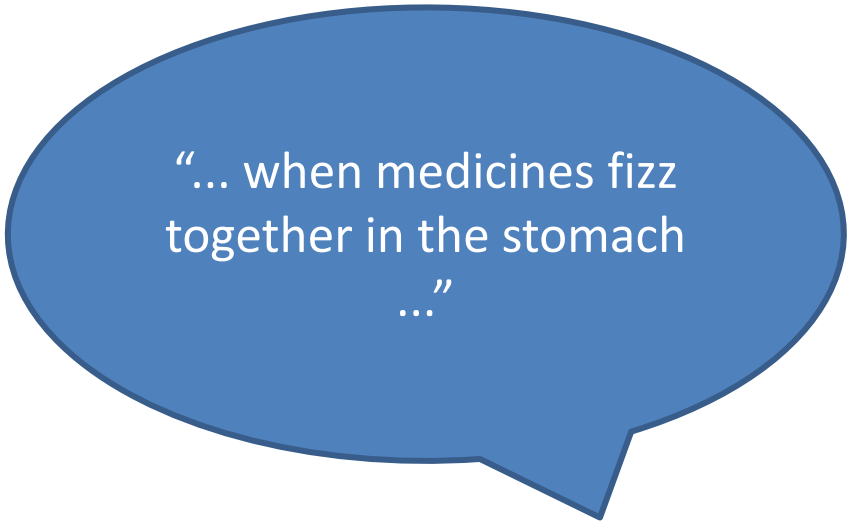
Recall	Recognise	Identify	Explain	Know
the mechanisms of drug interactions	available resources use to predict potential drug interactions	common drugs implicated in drug interactions	how to manage a drug interactions when prescribing	how to choose an appropriate drug to avoid a drug interaction

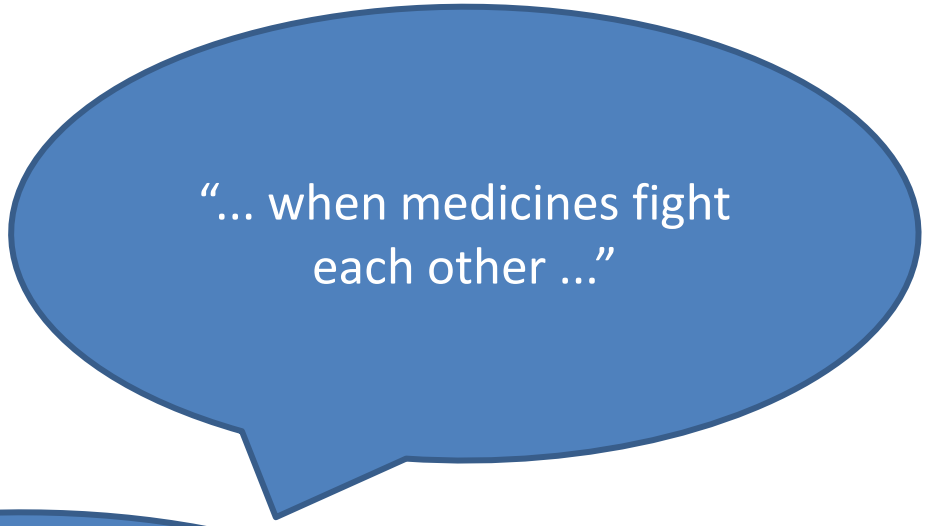
https://www.menti.com/6ds6m7cpqn

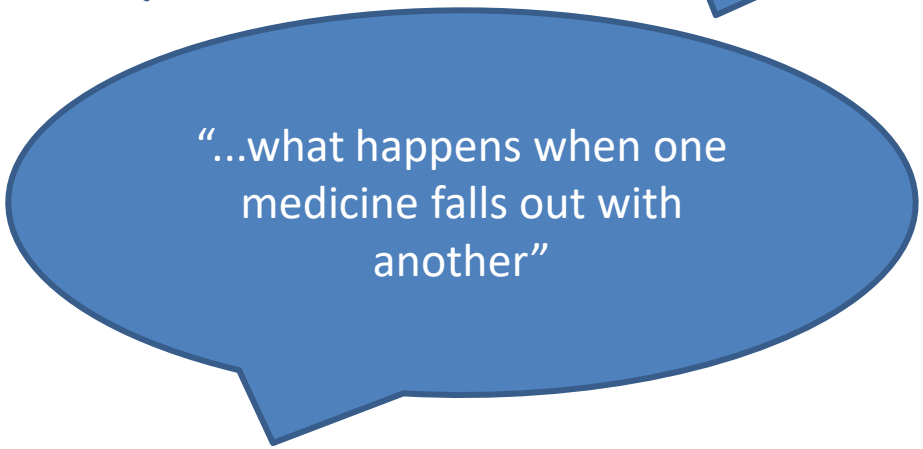


What is a Drug interaction ?

Definition by patients:







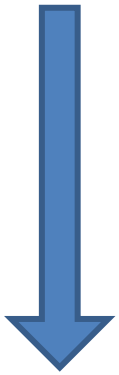
Definition of Drug interaction

“An interaction is said to occur when the effects of one drug are changed by the presence of another drug, herbal medicine, food, drink or by some environmental chemical agent” - Stockley's

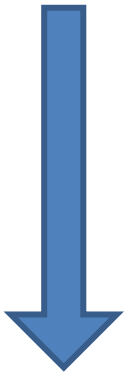
Incidence of drug interactions

- Approximately 3–26% of adverse reactions related to hospital admissions are due to drug-drug interactions
- Global prevalence of potentially inappropriate prescribing ranges from 13–35%
- Up to 11.1% of patients actually experience symptoms from drug interactions

Drug-drug interactions

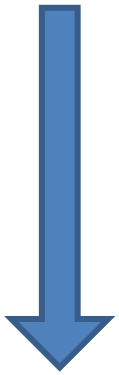


Major drug interactions

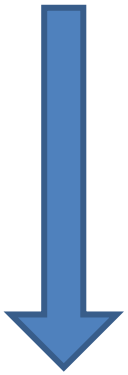


Moderate drug interactions

Drug-drug interactions



Increased toxicity

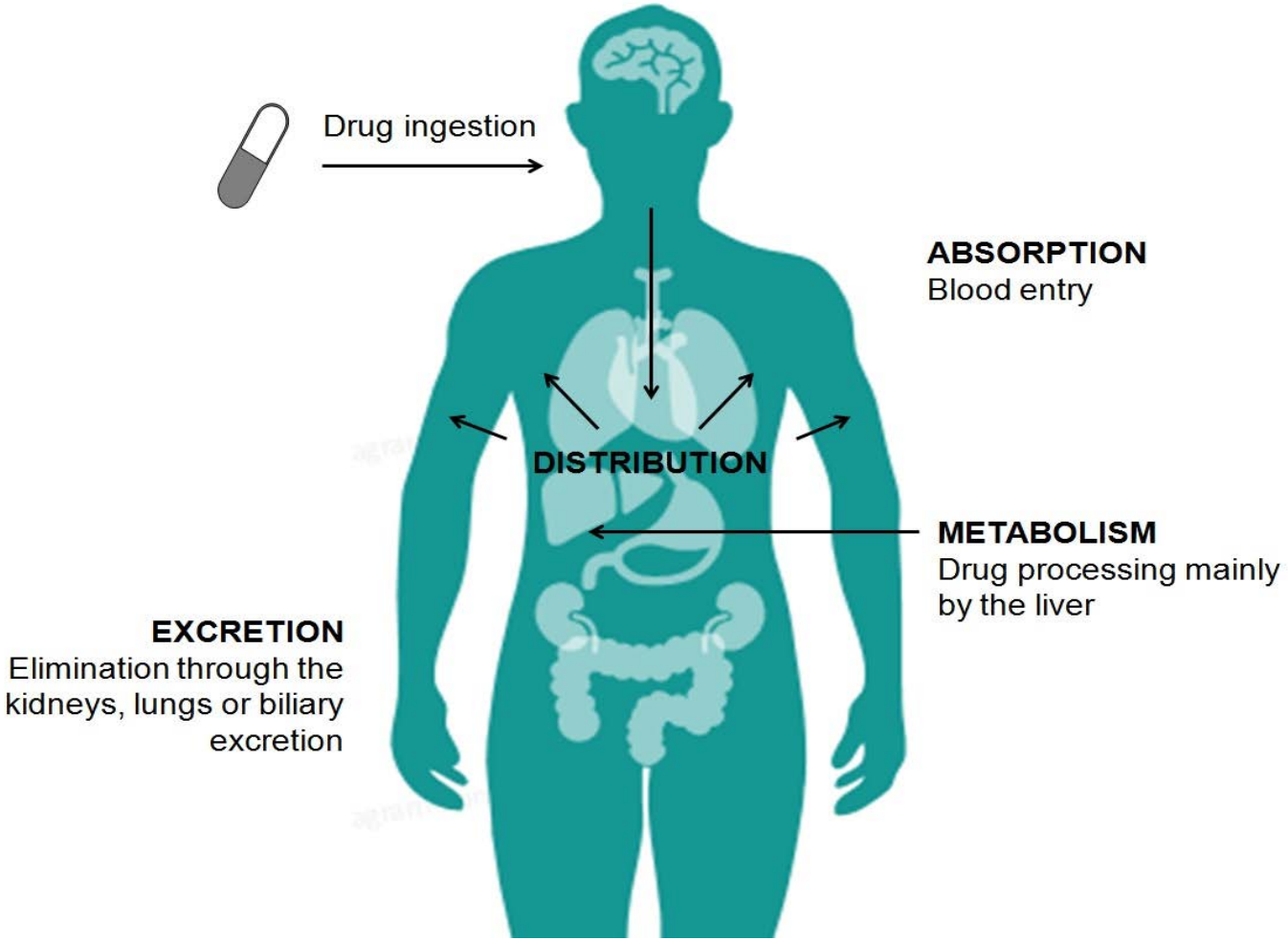


Reduced Efficacy

Types of drug interactions

- Drug-drug interaction
- Drug-food interaction
- Drug-disease interactions
- Drug-patient interactions
- Pharmaceutic drug interaction

Mechanism of Drug interactions: Pharmacokinetics



Mechanism of Drug interactions: Pharmacokinetics (1)

Absorption

- **Drugs forming complexes** in the GI tract examples:
  - tetracycline's form insoluble complexes with iron supplements/food/antacids
- **Change in gastrointestinal pH**
  - Ketoconazole needs acidic conditions for absorption. Antacid, H2 antagonist or PPI reduce acidity of the gut
- **Motility disorders**
  - Metoclopramide increase gastric transit and reduce time of contact between the drug and the GI membrane thereby reducing absorption

Mechanism of Drug interactions: Pharmacokinetics (2)

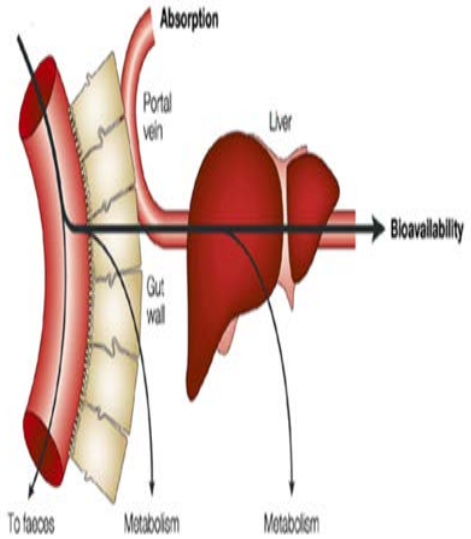
Distribution

- Drugs are distributed around the body by the systemic circulation
- Some proportion of drugs will bind to plasma protein
- Only unbound drug is available tissue sites for activity
  - Example Warfarin and diclofenac have same affinity for albumin, therefore the administration of diclofenac to a patient treated chronically with warfarin results in displacement of latter from its binding site.

Mechanism of Drug interactions: Pharmacokinetics (3)

Metabolism

- Enzyme inhibition by a drug/food can result in inhibition of the metabolism of another drug
  - Grapefruit juice, inhibits CYP3A4 therefore reduces the first-pass metabolism of calcium-channel blockers e.g., verapamil resulting in increased exposure
- Can also reduce the activity of pro-drugs
- Enzyme induction on the other hand results in decreased activity of another drug due to increased metabolism e.g., Rifampicin and warfarin



CRAP GPs spend all day on SICKFACES.com.

Cytochrome P450 Inducers

Carbemazepine
Rifampicin
Alcohol
Phenytoin
Griseofulvin
Phenobarbitone
Sulphonylureas

Cytochrome P450 Inhibitors

Sodium valproate
Isoniazid
Cimetidine
Ketoconazole
Fluconazole
Alcohol & Grapefruit juice
Chloramphenicol
Erythromycin
Sulfonamides
Ciprofloxacin
Omeprazole
Metronidazole

Mechanism of Drug interactions: Pharmacokinetics (4)

Excretion

- Most drugs are excreted either in the bile or in the urine , drug interaction affecting excretion could occur via:
  - **Changes to urine pH** reduces reabsorption by the renal tubules) e.g., Methotrexate and sodium bicarbonate increase excretion of methotrexate
  - **Competition for active transporters** leads to decreased clearance and thus higher plasma levels of drugs example penicillin and probenecid
  - **Reduction in renal blood flow** can consequently increase the reabsorption of certain drugs e.g., methotrexate reabsorption can be inhibited by NSAIDS

Pharmacodynamic drug interactions

- Effects of one drug are changed by the presence of another drug at its site of action or
- Indirect involving interference with physiological mechanisms
  - These interactions are much less easy to classify neatly than those of a pharmacokinetic type
- Pharmacodynamic drug interaction could either be
  - Antagonistic ; drugs can compete for the same receptor e.g., beta blockers propranolol and beta agonist salbutamol (antagonistic)
  - Additive e.g., aspirin and warfarin increased anticoagulation, salbutamol and diuretics increased risk of hypokalaemia

Pharmacodynamic drug interactions

More examples

- Additive:
  - Alcohol and CNS depressants
  - Anticholinergics and tricyclic antidepressants
  - Beta blockers and calcium channel blockers
- Antagonistic:
  - Temazepam and caffeine
  - Warfarin and vitamin K
  - Beta-blockers and salbutamol

Factors contributing to drug

Drugs with definite risk of haemolysis in most G6PD-deficient individuals

- Dapsone and other sulfones
- Fluoroquinolones (including ciprofloxacin, moxifloxacin, norfloxacin, and ofloxacin)
- Methylthioninium chloride
- Niridazole [not on UK market]
- Nitrofurantoin
- Pamaquin [not on UK market]
- Primaquine
- Quinolones
- Rasburicase
- Sulfonamides (including co-trimoxazole)

Drugs with possible risk of haemolysis in some G6PD-deficient individuals

- Aspirin
- Chloroquine
- Menadione, water-soluble derivatives (e.g. menadiol sodium phosphate)
- Quinine (may be acceptable in acute malaria)
- Sulfonylureas

Naphthalene in mothballs also causes haemolysis in individuals with G6PD deficiency.

When are drug interactions most likely to occur?

- When new drug is started
- When medication is stopped
- Interaction may not be seen immediately in drugs with long half-life e.g., amiodarone
- Mechanism of reaction often affects the timing
  - Enzyme inducers -1-3 weeks to maximum effect
  - Enzyme inhibitors- often within 24 hours

Prevention of Drug Interactions

- Asses clinical risk of your patient :
  - Critically ill patients who have multisystem disease with compromised renal, hepatic, cardiac, or pulmonary function have an increased risk for drug interactions
- Confirm and document patient's medication history
- Minimise the number of drugs being taken by frequently reviewing the patient's drug list
- Take extra caution when prescribing medications with a low therapeutic index (theses are known to have a high risk for drug interactions)
- Adverse drug interactions should be considered in the differential diagnosis whenever any change occurs in a patient's course

Drugs with low therapeutic index

- Anticoagulants
- Anti-arrhythmics
- Anticonvulsants
- Digoxin
- Lithium carbonate
- Oral hypoglycaemics
- Theophylline

Managing interactions

- Avoid the combination
  - Choose an alternative drug
  - Review the existing drug
- Adjust the dose
  - Of either or both interacting drug
- Monitor the patient
  - Patient characteristics
  - Concomitant illnesses
  - Timing and introduction of interacting drug
  - Expected time course of interaction
- Continue as before (do nothing)
  - If interaction is insignificant

Things to Remember

- Interactions are easily forgotten when prescribing
- Interactions are difficult to remember
- Pharmacodynamics interactions can often be predicted across drug classes
- Pharmacokinetic interactions can not be predicted – experiments needed
- Many interactions probably remain described – so look out for them
- The chances of interaction are 60 times higher in a patient taking 5 drugs than in one taking 2.

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British National Formulary (BNF)

Key information on the selection, prescribing, dispensing and administration of medicines.

Last updated:
26 May 2022
See what's changed

Drugs

Drug monographs describe the uses, doses, safety issues, medicinal forms and other considerations involved in the use of a drug.

Browse drugs by A to Z

A | B | C | D | E | F | G | H

I | J | K | L | M | N | O | P

Q | R | S | T | U | V | W | X

Y | Z

Treatment summaries

Browse an A to Z list of treatment summaries covering:

- drug use related to a particular body system
- drug management or treatment of common conditions
- comparisons between groups of drugs.

View treatment summaries A to Z

Interactions

Check for drug interactions. Includes information on the severity of an interaction and the type of evidence to support it.

View interactions A to Z

Medicines guidance

General guidance on prescribing and the use of medicines. Includes guidance on prescribing in palliative care, prescription writing and prescribing in renal impairment.

Wound management

Wound management products and elasticated garments. Browse by wound type or product type.

Medical devices

Borderline substances

Apixaban

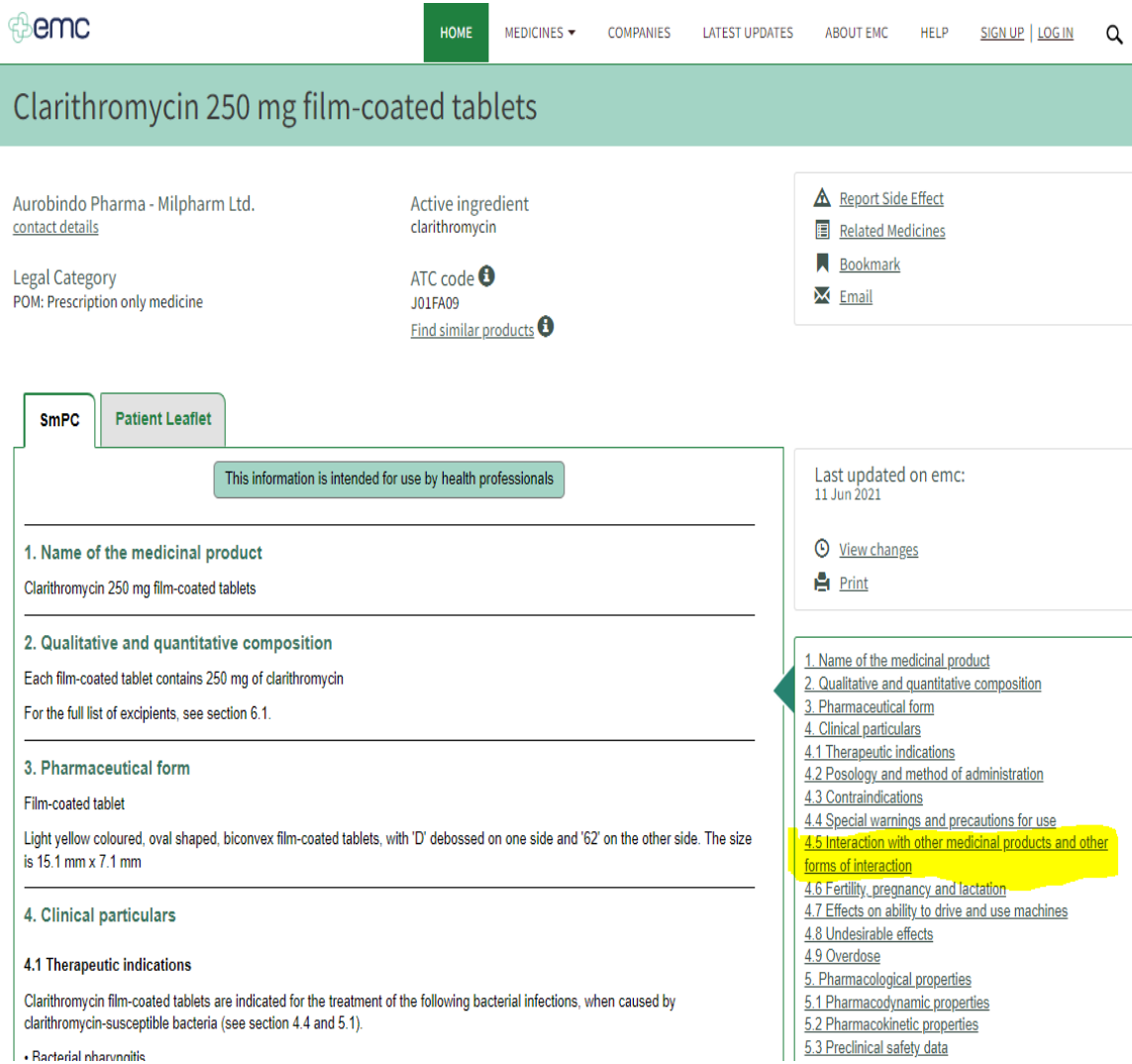
Navigate to section

Interactions

View interactions for apixaban

Medicinal forms and pricing

There can be variation in the licensing of different medicines containing the same drug.



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Clarithromycin 250 mg film-coated tablets

Aurobindo Pharma - Milpharm Ltd.
contact details

Active ingredient
clarithromycin

Legal Category
POM: Prescription only medicine

ATC code
J01FA09
Find similar products

Report Side Effect
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This information is intended for use by health professionals

1. Name of the medicinal product

Clarithromycin 250 mg film-coated tablets

2. Qualitative and quantitative composition

Each film-coated tablet contains 250 mg of clarithromycin

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet

Light yellow coloured, oval shaped, biconvex film-coated tablets, with 'D' debossed on one side and '62' on the other side. The size is 15.1 mm x 7.1 mm

4. Clinical particulars

4.1 Therapeutic indications

Clarithromycin film-coated tablets are indicated for the treatment of the following bacterial infections, when caused by clarithromycin-susceptible bacteria (see section 4.4 and 5.1).

• Bacterial pharyngitis

Last updated on emc:
11 Jun 2021

View changes
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