



# Management of different types of drug interactions

Lenka Součková

# Learning outcomes

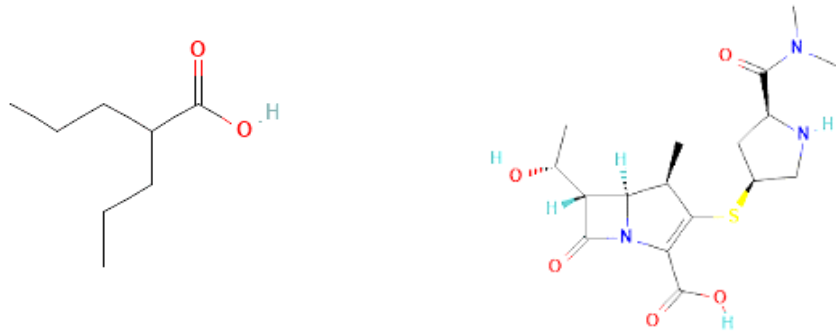
- The student identifies possible causes of drug interactions.
- The student will explain the connections between the drug interaction and the adverse drug reaction.
- The student will recognize the clinical severity of a drug interaction.
- The student will present various proposals for management of drug interactions.

# Lecture content

- Description and evaluation of drug interaction
- Scenario 1-5 and suggestions for different drug interaction solutions
- Conclusion

# Drug interaction

## Valproic acid and meropenem



[Valproic Acid | C8H16O2 | CID 3121](#)  
- [PubChem \(nih.gov\)](#)

[Meropenem | C17H25N3O5S | CID 441130](#)  
- [PubChem \(nih.gov\)](#)

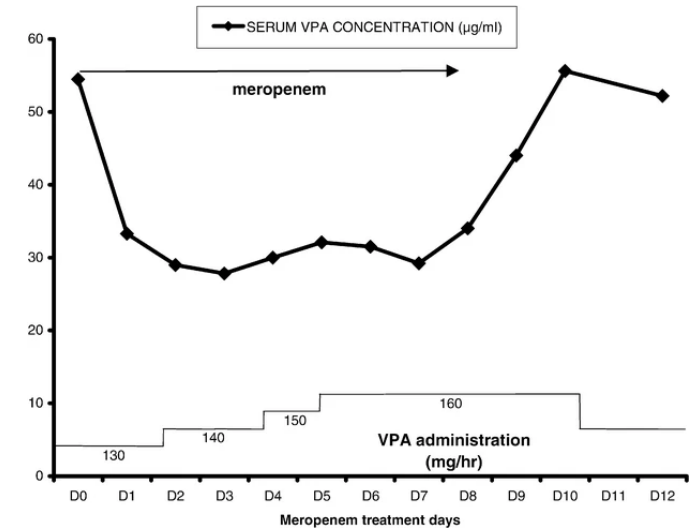
Decreases in blood levels of valproic acid have been reported when it is co-administered with *carbapenem agents* resulting in a 60-100 % decrease in valproic acid levels in about two days. Due to the rapid onset and the extent of the decrease, co-administration of carbapenem agents in patients stabilised on valproic acid is not considered to be manageable and therefore should be avoided (see section 4.4).

[Convulex 500 mg Capsules - Summary of Product Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#)

Applied and clinical pharmacology (aVLKF091)

Reference range: 50-100  $\mu\text{g/ml}$

The screenshot shows a search engine interface with the query 'valproic acid and drug interaction and meropenem'. Below the search bar, there are navigation options: 'Vše', 'Obrázky', 'Knihy', 'Zprávy', 'Videa', 'Více', and 'Nástroje'. The search results indicate 'Přibližný počet výsledků: 67 600 (0,44 s)'.



[Pharmacokinetic interaction between valproic acid and meropenem | SpringerLink](#)

# Drug interaction – Meropenem and valproic acid

## Scenario 1

- A patient on long-term treatment with valproic acid 500 mg/12 h admitted to the ICU was given meropenem 2 g/8 h.
- Convulsions were observed after 2 doses of meropenem, and the dose of valproic acid was increased empirically by 1000 mg/12 h.
- A blood sample was taken for TDM to determination of valproic acid level.
- Laboratory results – 20 µg/ml.
- The dose of valproic acid was increased to 1000 mg/8 hours, after control the level was 16 µg/ml.
- Valproic acid was changed to levetiracetam 1500 mg/12 h.

# Drug interaction – Meropenem and valproic acid

## Scenario 2

- A patient on long-term treatment with valproic acid 500 mg/12 h admitted to the ICU was indicated for treatment with meropenem 2 g/8 h.
- Here, they were familiar with the drug interaction and it was suggested to replace meropenem with imipenem/cilastatin 1000 mg/6 h.
- Convulsions were observed after 2 doses of imi/cila and the dose of valproic acid was increased empirically.
- A blood sample was taken for TDM and determination of the valproic acid level
- Laboratory results – 20 µg/ml
- Valproic acid was replaced by levetiracetam 1500 mg/12 h.
- Imi/cila was switched to tigecycline at an initial dose of 100 mg, followed by 50 mg/12 h.

# Drug interaction – Meropenem and valproic acid

## Scenario 3

- A patient on long-term treatment with valproic acid admitted to the ICU was indicated for treatment with meropenem.
- Here they were aware of the drug interaction and an alternative to the carbapenem ATB levofloxacin was suggested, but in the end, due to the risk of CNS infection, ceftazidime 2 g/8 h was administered.
- Valproic acid level control – 60 µg/ml.

# Drug interaction – Meropenem and valproic acid

## Scenario 4

- A patient on long-term treatment with valproic acid admitted to the ICU was indicated for treatment with meropenem.
- Here they were aware of the drug interaction and an alternative to valproic acid was suggested and the patient was switched to levetiracetam 1500 mg/12 h even before starting antibiotic therapy.
- Treatment with meropenem 1 g/6 h in prolonged infusion was started.



# Drug Interaction – Meropenem and valproic acid

## Scenario 5

- Severe valproic acid intoxication treated with off-label meropenem.



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## Treatment of valproic acid overdose with meropenem in an epileptic patient

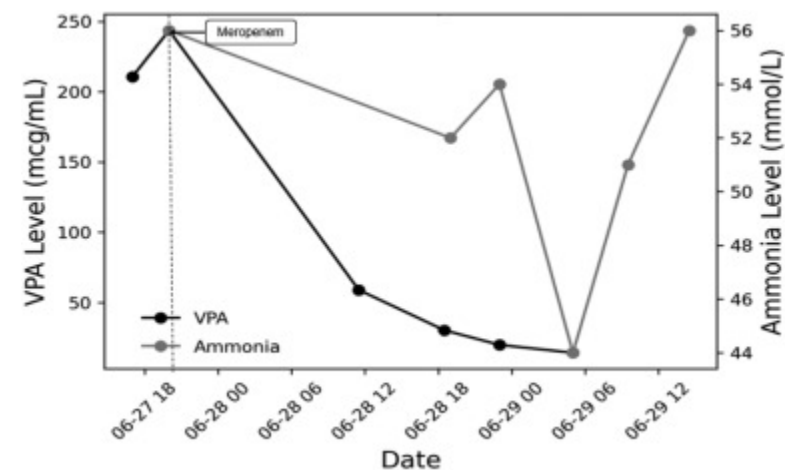
David Cunningham Pharm. D<sup>a</sup> , Kacie Clark Pharm. D<sup>b</sup>  , Kito Lord MD, MBA<sup>c</sup> 

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<https://pubmed.ncbi.nlm.nih.gov/34625331/>

# Take home message

- In the management of drug interactions must be considered
  - Clinical relevance of drug interaction
  - Potential severity
  - It is advisable to prevent the occurrence of ADR as a result of drug interactions
  - There are always several solutions to choose from, and the optimal one should be chosen with regard to the needs of a particular patient
- Management of significant drug interactions may include
  - Reassessing existing treatments in interaction prevention
  - Reevaluation of a new, intended therapy
  - Adjusting the dosage of medicines
  - Monitoring of effect, adverse effect, monitoring of plasma concentration and TDM
  - Consultation of a clinical pharmacologist/pharmacist

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