AETC AIDS Education & Training Center Program Mountain West

Clinically Relevant Drug Interactions with Direct Acting Antivirals (DAAs)

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Disclosures

Nothing to disclose

Objectives

- Describe basic pharmacokinetic properties of DAAs
- Identify clinically important interactions between the DAAs and
  - Antiretroviral medications
  - Non-HIV medications
- Apply outcomes from drug interaction tools to patient care to modify treatment of HCV or HIV

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CASE 1

- TC is a 50-year-old male newly diagnosed with HIV (pan-sensitive genotype, CD4 count 350 cells/mm3 and VL 50,000). Hepatitis serologies are:
  - HCV Ab positive – GT3 / VL 4,000,000
  - Hepatitis B surface Ab positive / core negative
  - Hepatitis A total Ab positive
- Kidney function is normal, other labs do not indicate the patient has cirrhosis.

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CASE 1

- Keeping in mind you want to treat the HCV in the next 6-12 months, what ART would you select?
  A. Dolutegravir (Tivicay®) + Emtricitabine/Tenofovir DF (Truvada®)
  B. Bictegravir/Emtricitabine/Tenofovir AF (Biktarvy®)
  C. Dolutegravir/Lamivudine (Dovato®)
  D. Darunavir/Cobicistat/ Emtricitabine/Tenofovir alafenamide (Symtuza®)

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Basic PK Properties of DAAs

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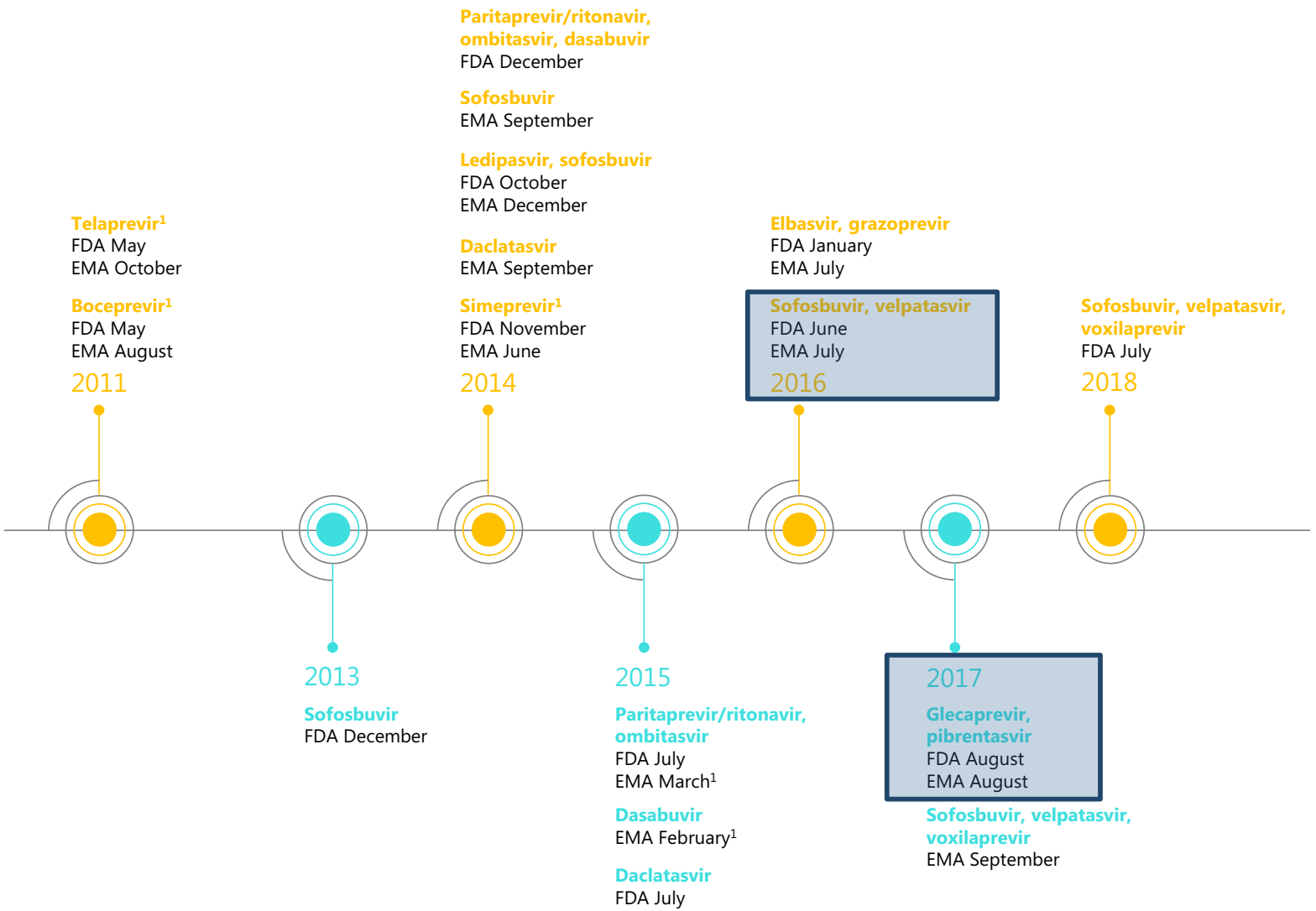

Smolders et al. Viral Hepatitis C Therapy: Pharmacokinetic and Pharmacodynamic Considerations: A 2019 Update. Clinical Pharmacokinetics (2019) 58:1237–1263

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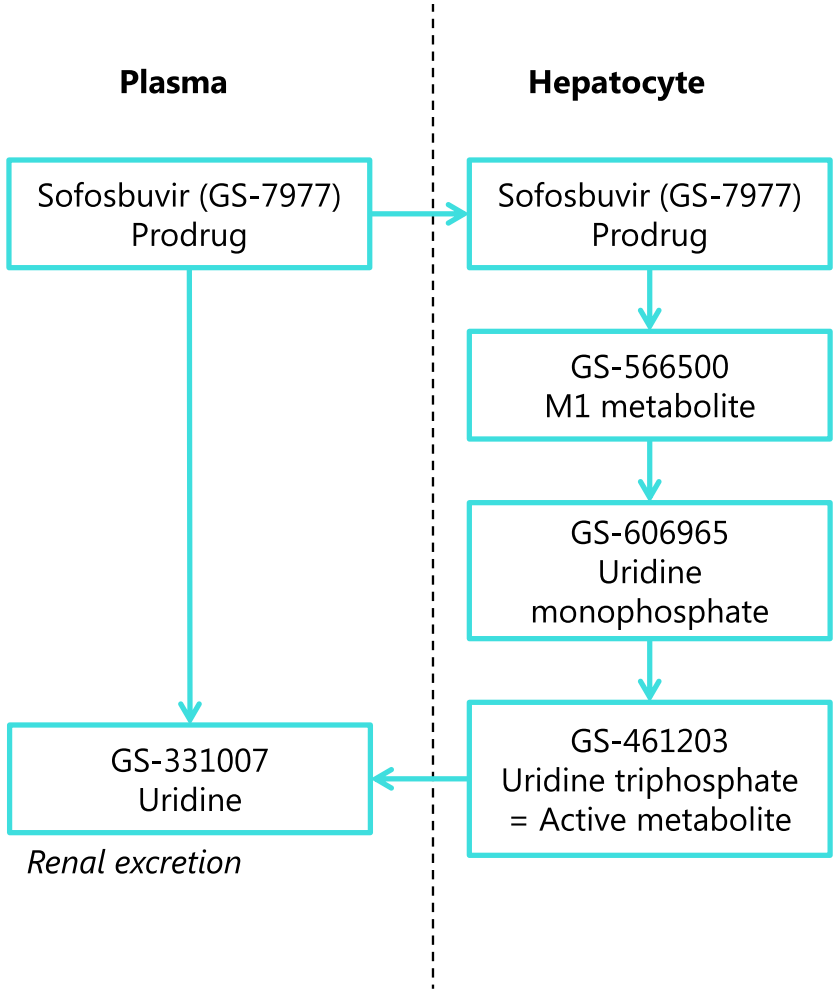
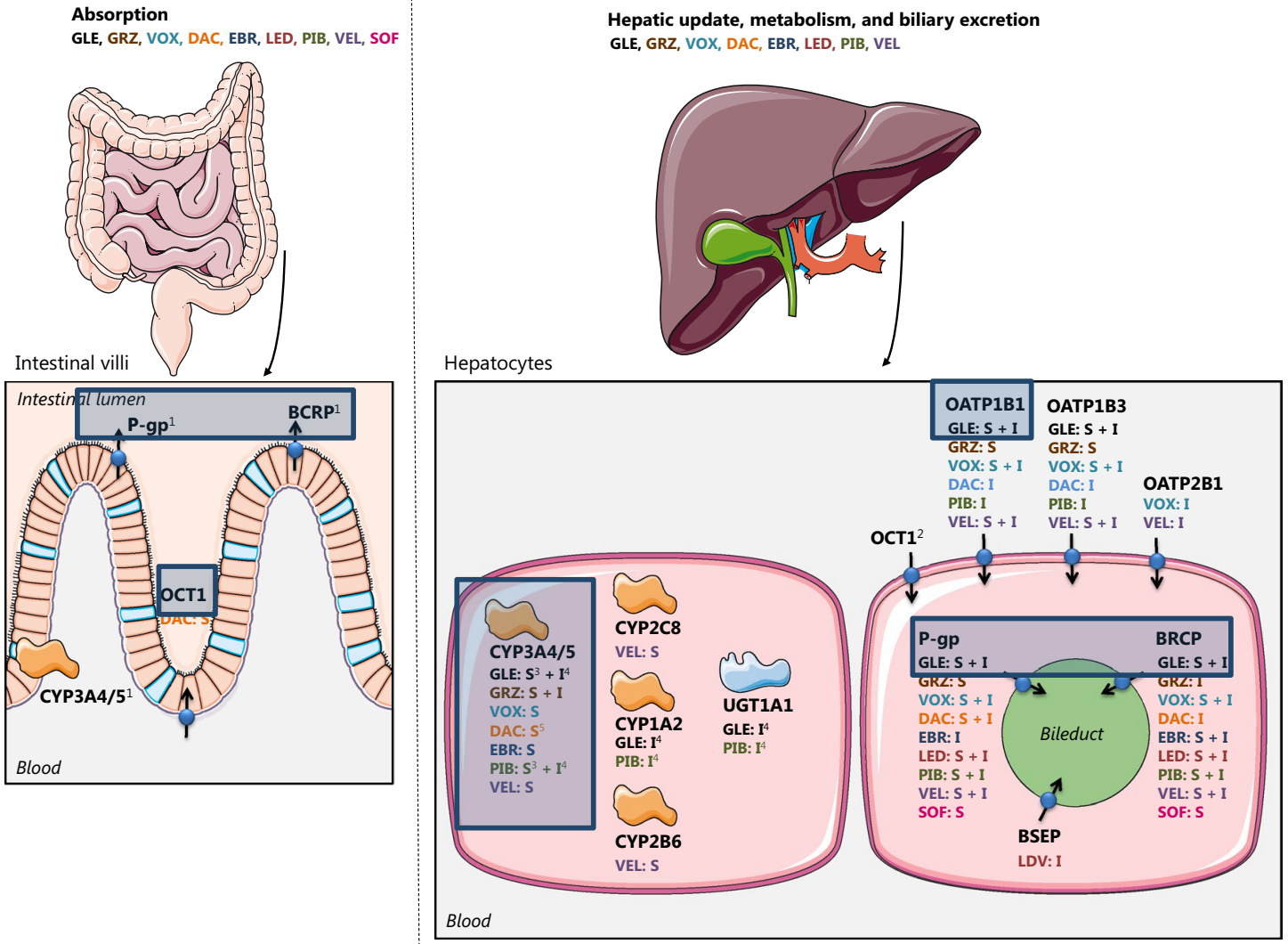
Pharmacokinetics

- SOF/VEL (Epclusa®)
  - Absorption
    - VEL has a **pH dependent solubility**
  - Metabolism
    - SOF: Substrate fort PgP
    - VEL: **substrate for CYP3A (major)**, 2B6 and 2C8
- GLE/PIB (Mavyret®)
  - Absorption
    - Food enhances absorption
  - Metabolism
    - GLE: **substrate for CYP3A4**



Deep Dive



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DAA and ARV Interactions

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CASE 2

- MT is a 60-year-old male well controlled on a salvage regimen of darunavir/cobicistat (Prezcobix) + Bictegravir/Emtricitabine/Tenofovir AF (Biktarvy®) and needs to be treated for GT 1 (naïve without cirrhosis). Which of the following would be the best treatment option for this patient?
  A. Glecaprevir/Pibrentasvir (Mavyret®)
  B. Sofosbuvir/Velpatasvir (Epclusa)
  C. Something else

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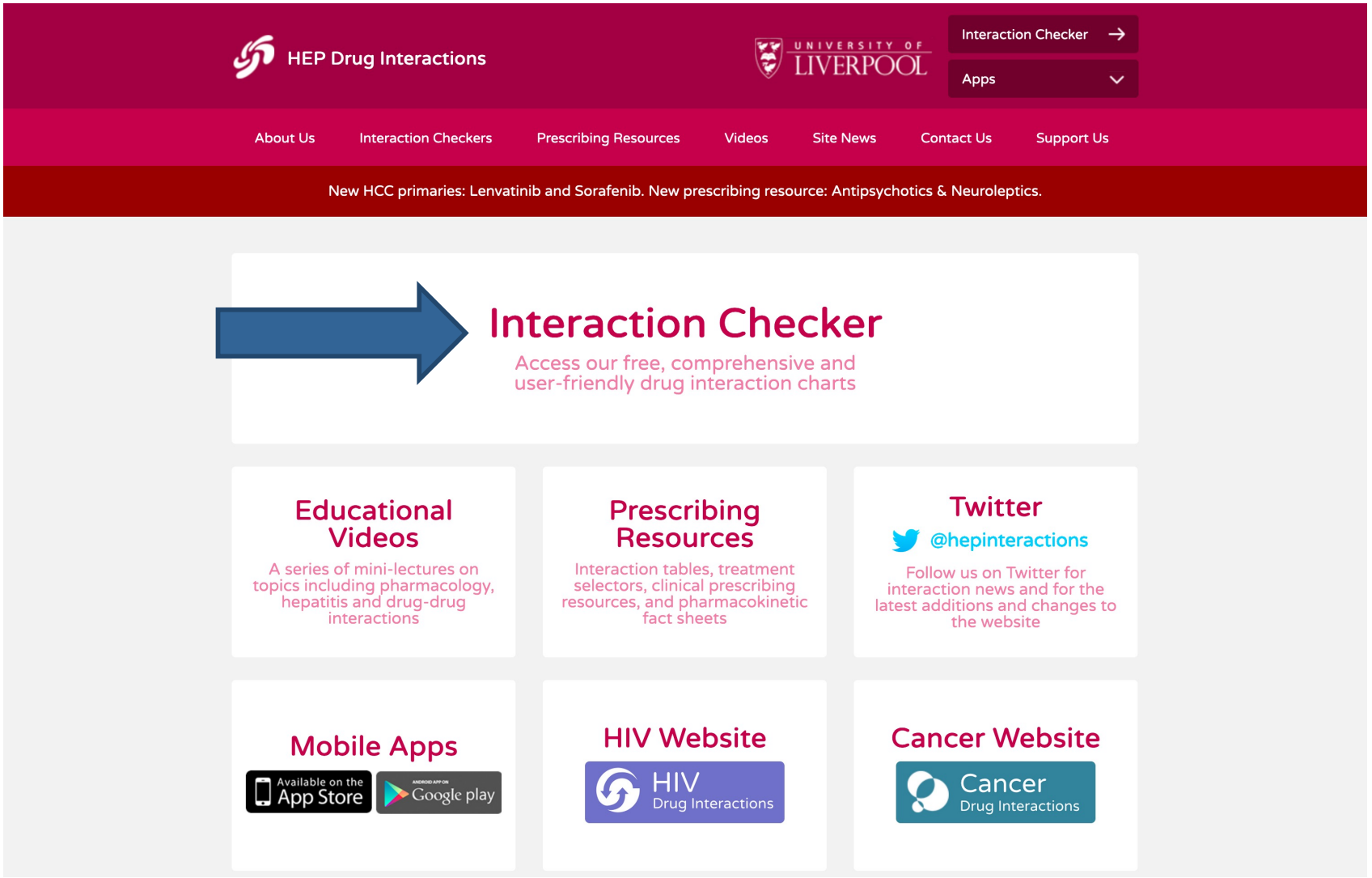
Navigating Interactions



https://www.hep-druginteractions.org/

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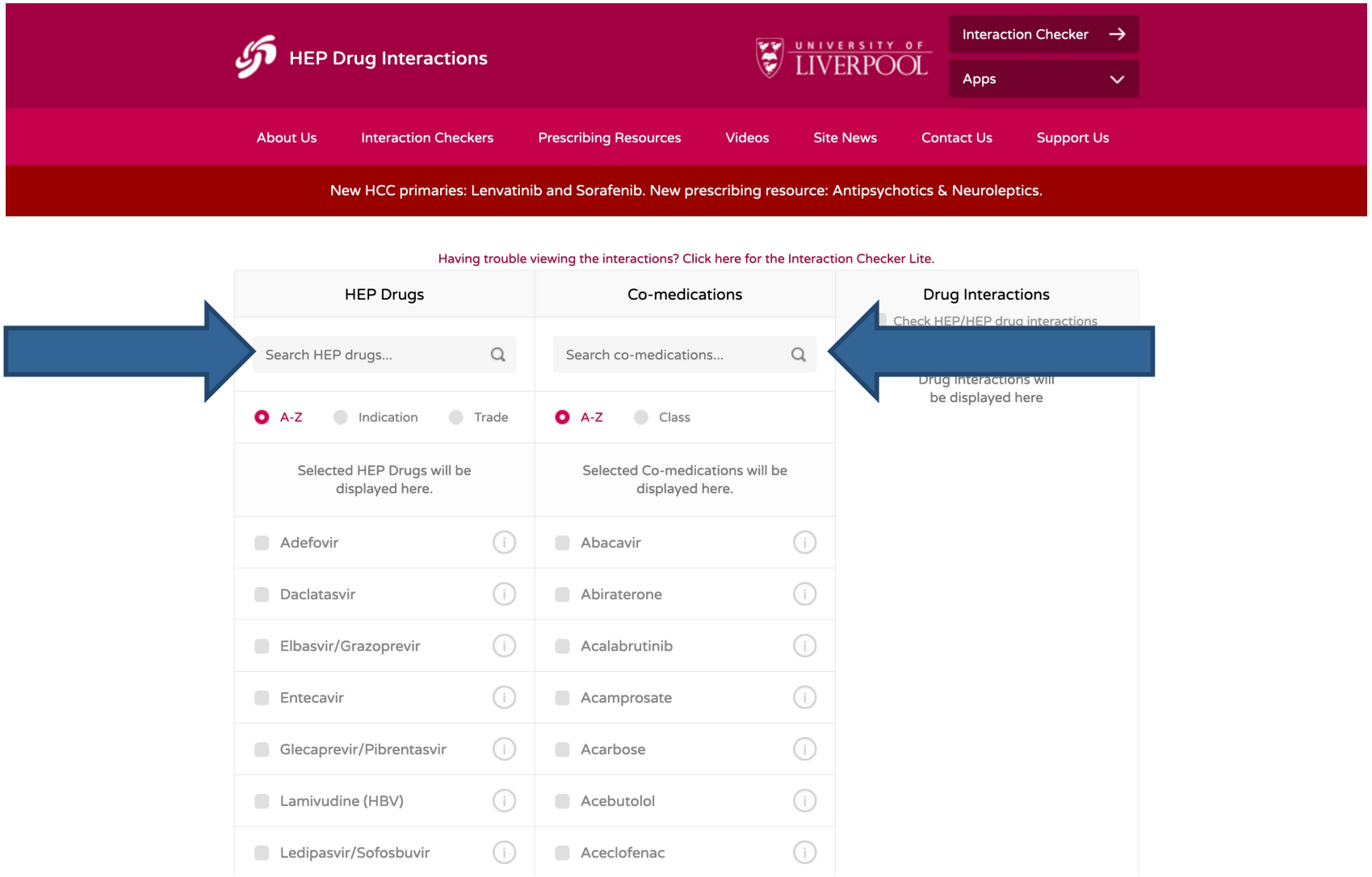
Navigating Interactions



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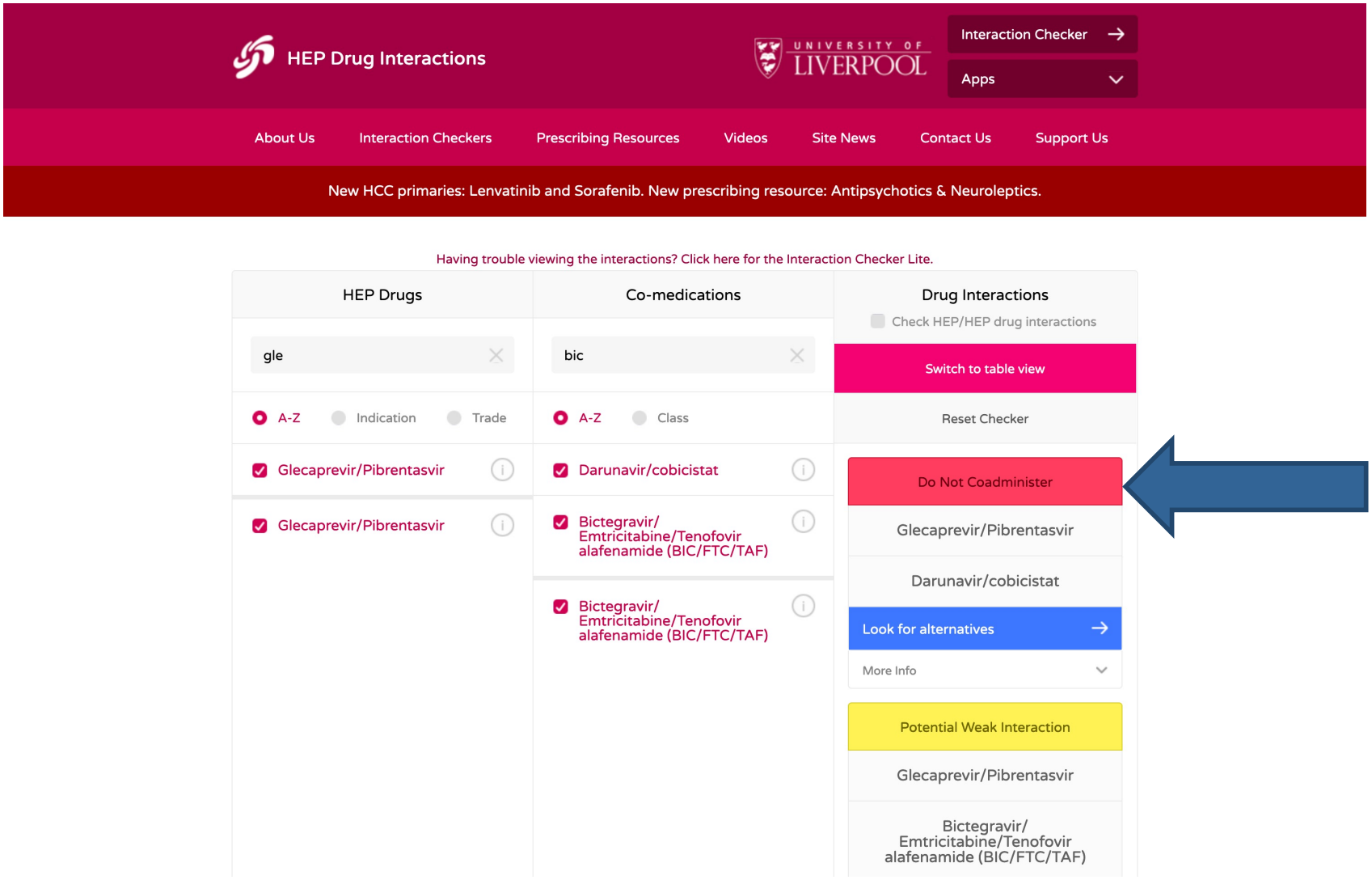
Navigating Interactions



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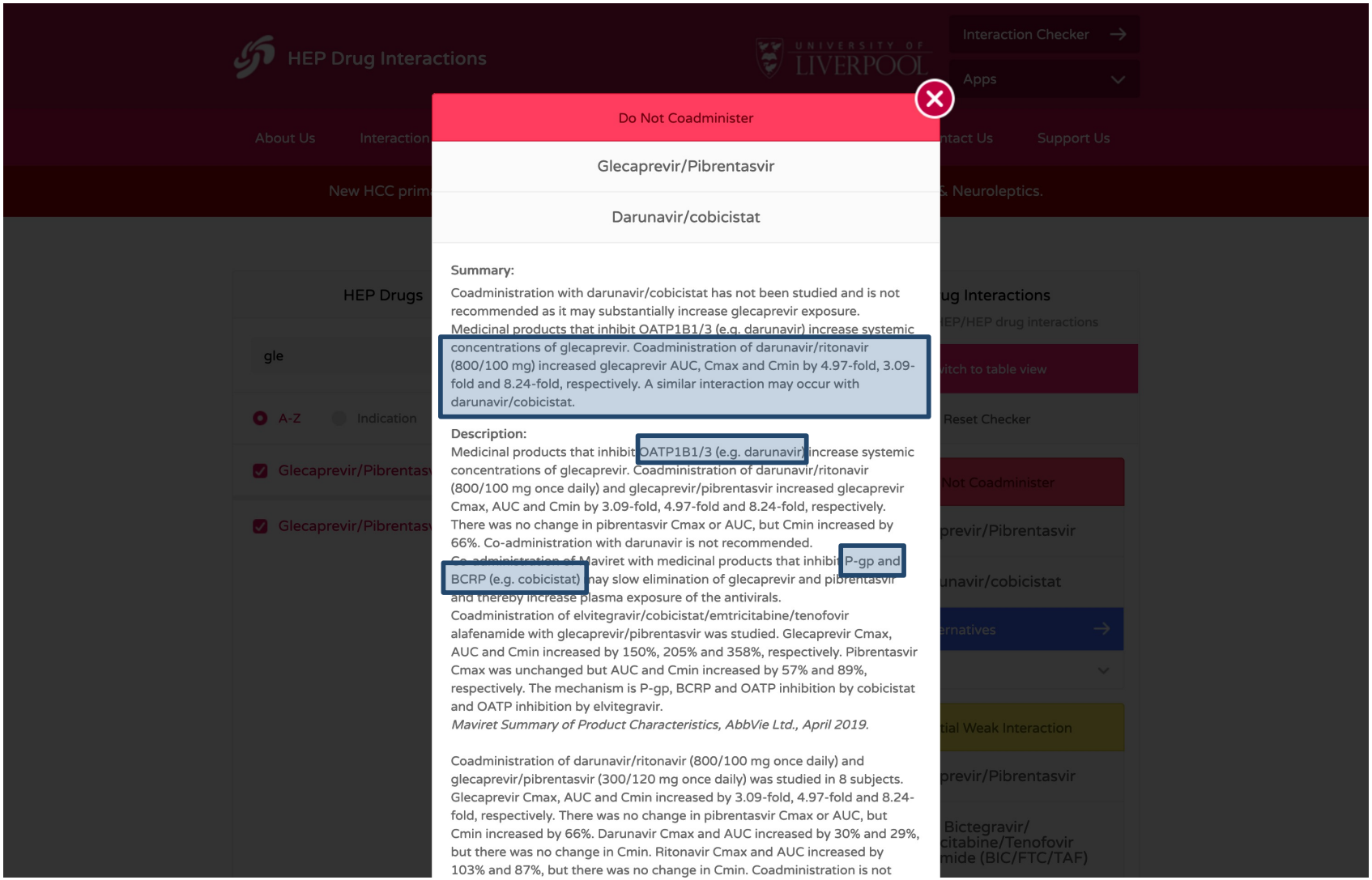
Navigating Interactions



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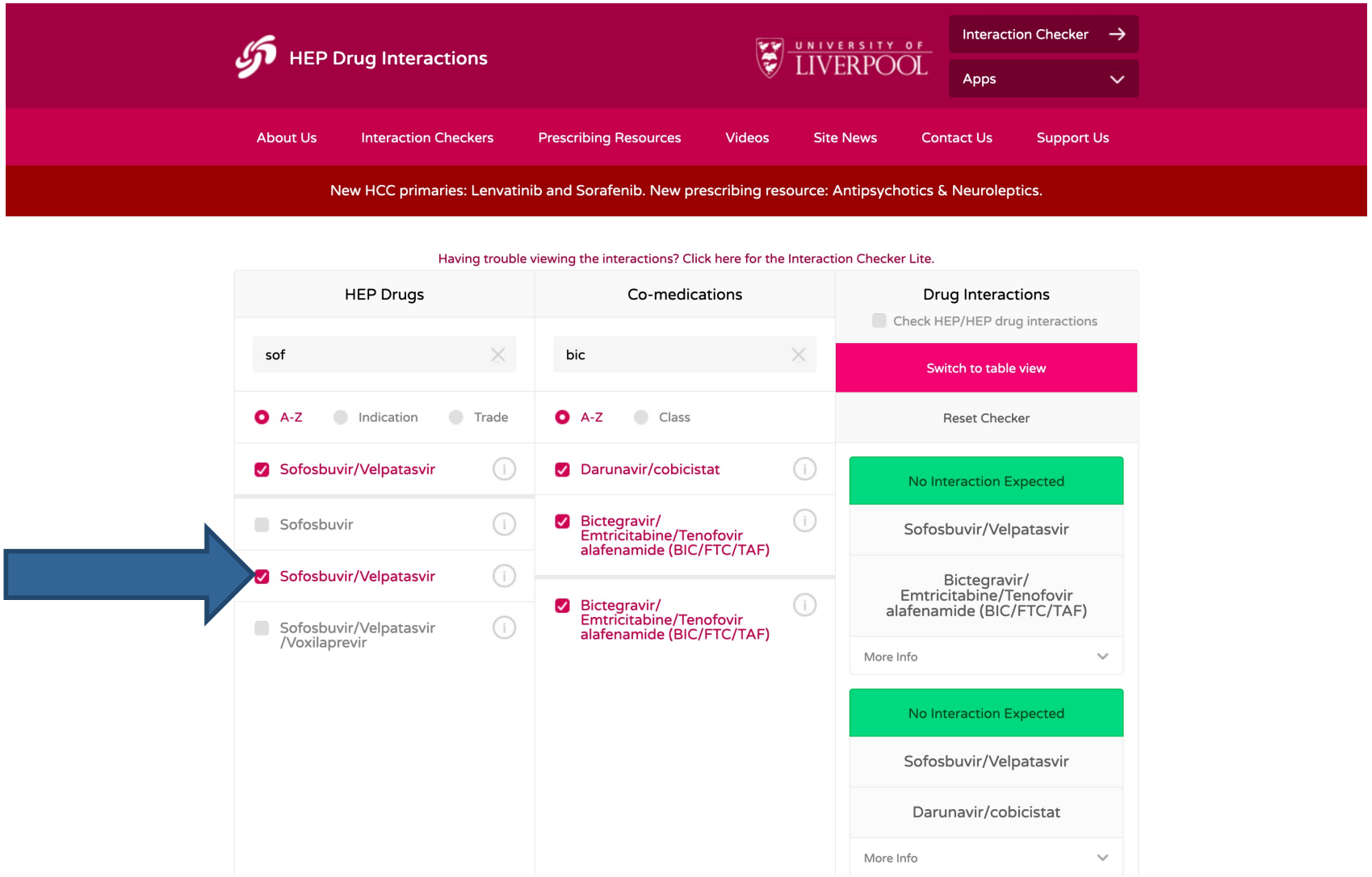
Navigating Interactions



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DAA and ARV Interactions

DAA	Avoid/Not Recommended	Use with caution or adjust dose/timing
Glecaprevir/pibrentasvir	Efavirenz and etravirine (decrease G/P) Boosted atazanavir and darunavir (increase G/P)	
Sofosbuvir	Tipranavir/ritonavir (decrease SOF through PgP)	
Velpatasvir	Efavirenz, etravirine, tipranavir/ritonavir (decrease VEL)	Avoid TDF if possible (increases TDF), especially with ritonavir or cobicistat (TAF ok)

Adapted from: MacBrayne CE et al. CID 2016. Additions made based on prescribing info and Liverpool HEP Interactions.

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DAAs and Non-ARV Interactions

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CASE 3

- MH is a 35-year-old female with HIV and well controlled on Bictegravir/Emtricitabine/Tenofovir AF (Biktarvy®). She takes EE/Levonorgestrel (various) and omeprazole 40 QD for control of her Barrett's Esophagus and you are considering treating her HCV with either G/P or SOF/VEL. Which of the following interactions would be the most significant?
  A. Increase in EE levels from G/P
  B. Decrease in SOF levels from omeprazole
  C. Decrease in Glecaprevir levels from omeprazole
  D. Increase in EE levels from SOF/VEL

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Drug Class	Glecaprevir/Pibrentasvir (Mavryet®)	Sofosbuvir/Velpatasvir (Epclusa)
Acid Reducing Agents	No interaction	VEL solubility decreases as pH increase • Separate antacids by 4 hours • Administer with H2RA OR separate by 12 hours (~40mg famotidine BID) • **Not recommended with PPIs**
Amiodarone	Use with caution	Significant bradycardia
Anticonvulsants: Carbamazepine, phenytoin, PHB	↓ **G/P (not recommended)**	↓ **SOF/VEL (not recommended)**
Antimycobacterial: Rifabutin, rifampin, rifapentine	↓ **G/P (not recommended)**	↓ **SOF/VEL (not recommended)**
Statins	↑ **Lovastatin (Avoid)** ↑ **Simvastatin (Avoid** ↑ **Atorvastatin (Avoid)** ↑ Rosuvastatin (10 mg max) ↑ Pravastatin (↓ dose 50%) ↑ Pitavastatin (Lowest dose) ↑ Fluvastatin (Lowest dose)	↑ Rosuvastatin (10 mg max) ↑ Atorvastatin (monitor)
Oral Contraceptives	↑ EE levels (avoid or monitor LFTs)	
St Johns Wort	↓ **G/P (not recommended)**	↓ **SOF/VEL (not recommended)**

Package inserts / Liverpool

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Acknowledgment

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