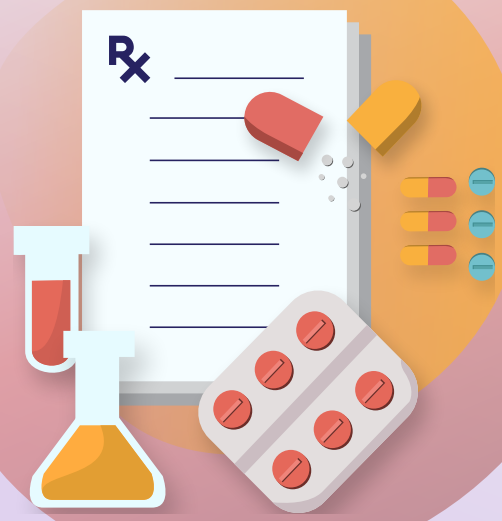
Drug Dosing in Cirrhosis



A systematic approach to symptom assessment, includes the impact on function and quality of life

All drug dosing needs to be carefully considered in patients with liver dysfunction and cirrhosis due to the following alterations we see in this patient population:

- **Decreased drug clearance due to liver cell necrosis.** Net loss of cytochrome P450 enzymes, a reduction in first pass metabolism of medications and higher plasma concentrations.
- **Hypoalbuminemia.** Increased serum concentrations in medications with high protein binding.
- **Ascites**. Increased volume of distribution, affecting medications with hydrophillic drug properties.
- **Decreased hepatic blood flow.** Increased serum levels and higher bioavailability.
- **Impaired renal and biliary excretion.** Increased plasma concentrations of medications.

Practical tips to consider when starting a medication in cirrhosis:

- Start with lower doses, and consider less frequent dosing (e.g. every other day dosing).
- Consider specialty compounding pharmacies when you require a dose lower than what is commercially available.
- Determine your patients Child Pugh status and see if a medication monograph has any guidance based on the degree of liver dysfunction.
- Look at the pharmacokinetic properties of a medication. This can be found in product monographs or tertiary drug resources. Focus on drug metabolism: is the drug extensively metabolized by hepatic routes or renal routes? Is it highly protein bound (i.e. >90%).
- Look at your individual patient's physiological characteristics and consider how this will this affect drug metabolism. See the list above for common effects on medication plasma concentrations. Consult your pharmacist for more complex guidance/discussion.
- Monitor clinical effects and hepatic indices (eg: LFT's, bilirubin, albumin, coagulation studies) frequently.

Within Alberta, the following resources are available through AHS via the Knowledge Resource Services (KRS) portal:

- **Liver tox –** NIH resource which provides information on the potential for and presentation of drug-induced liver injury
- **Lexicomp –** contains drug pharmacokinetic/pharmacodynamic information, drug interactions.