Palliative care support for prescribing in end-stage liver disease

Learn how treatment guidance from the Palliative Care Formulary is used by healthcare professionals to treat and manage the symptoms and common side effects of a patient with hepatic impairment.

Independent, specialist information, grounded in clinical practice

Palliative Care Formulary

Available through

Medicines Complete

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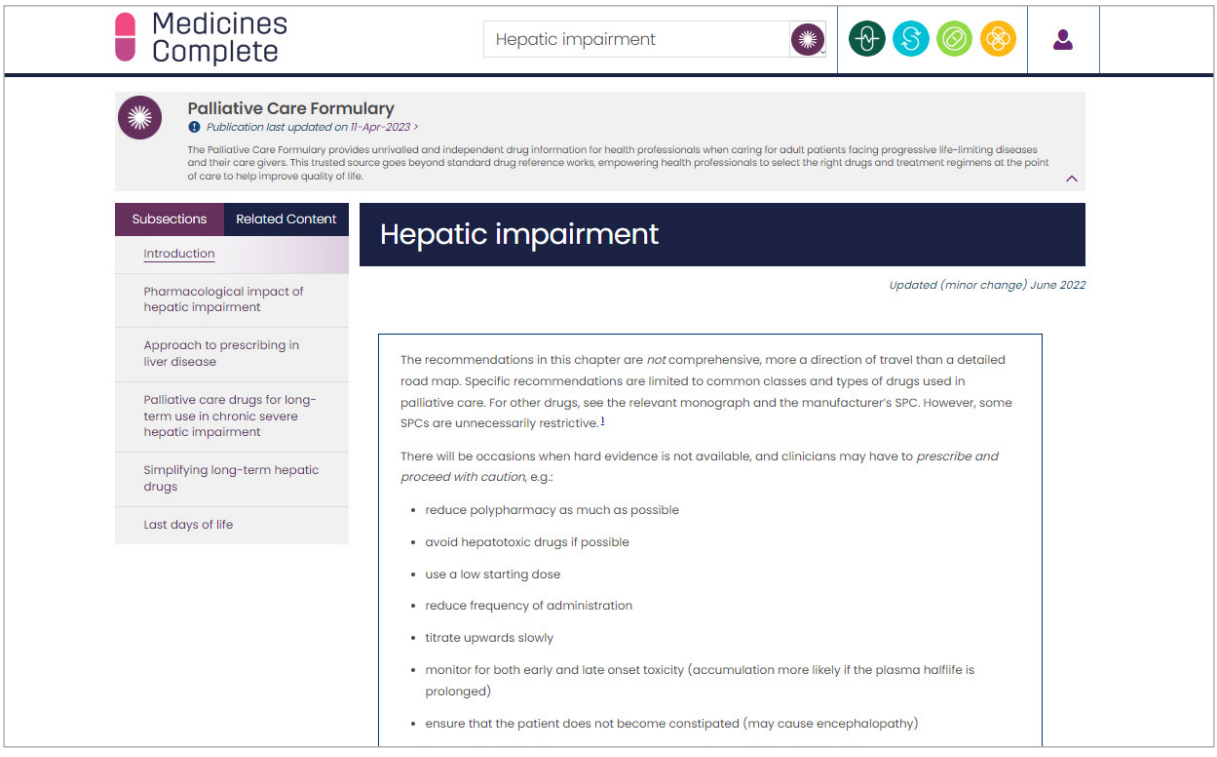
Using essential knowledge at the point of care

John is a 55-year old man with end-stage liver disease as a result of long-term excessive alcohol consumption. A liver transplant is not an option and he has been referred to palliative care for symptom control.

PCF Hepatic impairment chapter provides details of chronic liver disease and the associated complications of hepatic encephalopathy, ascites and hepatorenal syndrome.



The multidisciplinary palliative care team review John's case and discuss the planned treatment strategy. They are less familiar with treating patients with chronic severe hepatic impairment at the end of life. They want to know more about prescribing considerations for this group of patients.

How does end-stage liver disease affect the pharmacological impact of drugs?

The liver is the main site for the metabolism of most drugs. Although the hepatic reserve is large, chronic severe decompensated hepatic impairment (end-stage liver disease) affects the intrinsic activity and capacity of the metabolising enzymes, potentially leading to toxicity with hepatically metabolised drugs. Hepatic impairment can also cause changes within the body which can affect the absorption, distribution and elimination of drugs altering their action or overall clearance. Pharmacodynamic changes and secondary phenomena, e.g. altered receptor sensitivity, ascites, coagulopathy, hepatic encephalopathy, disruption of the blood-brain barrier and renal impairment can also affect the impact of drugs.

What considerations are needed when prescribing for patients with chronic severe hepatic impairment?

Hard evidence for specific dose recommendations is limited and the use of drugs in severe hepatic impairment may be off-label and/or contra-indicated. When deciding drug doses in hepatic impairment, it is important to consider the patient's overall clinical condition, rate of deterioration and goals of care, and not rely solely on liver function tests.

Essential drugs should not be withheld but high-risk patients should be closely monitored. Where drugs are deemed essential the following guidance is pragmatic:

- reduce polypharmacy as much as possible
- avoid hepatotoxic drugs if possible
- use a low starting dose
- reduce frequency of administration
- titrate upwards slowly
- monitor for both early and late onset toxicity (accumulation is more likely if the plasma half-life is prolonged)
- ensure that the patient does not become constipated (may cause hepatic encephalopathy)
- beware of sedation (may cause, worsen or mask hepatic encephalopathy).

PCF Hepatic impairment chapter provides details of the impact of hepatic impairment on drug pharmacology and general guidance on the approach to prescribing.

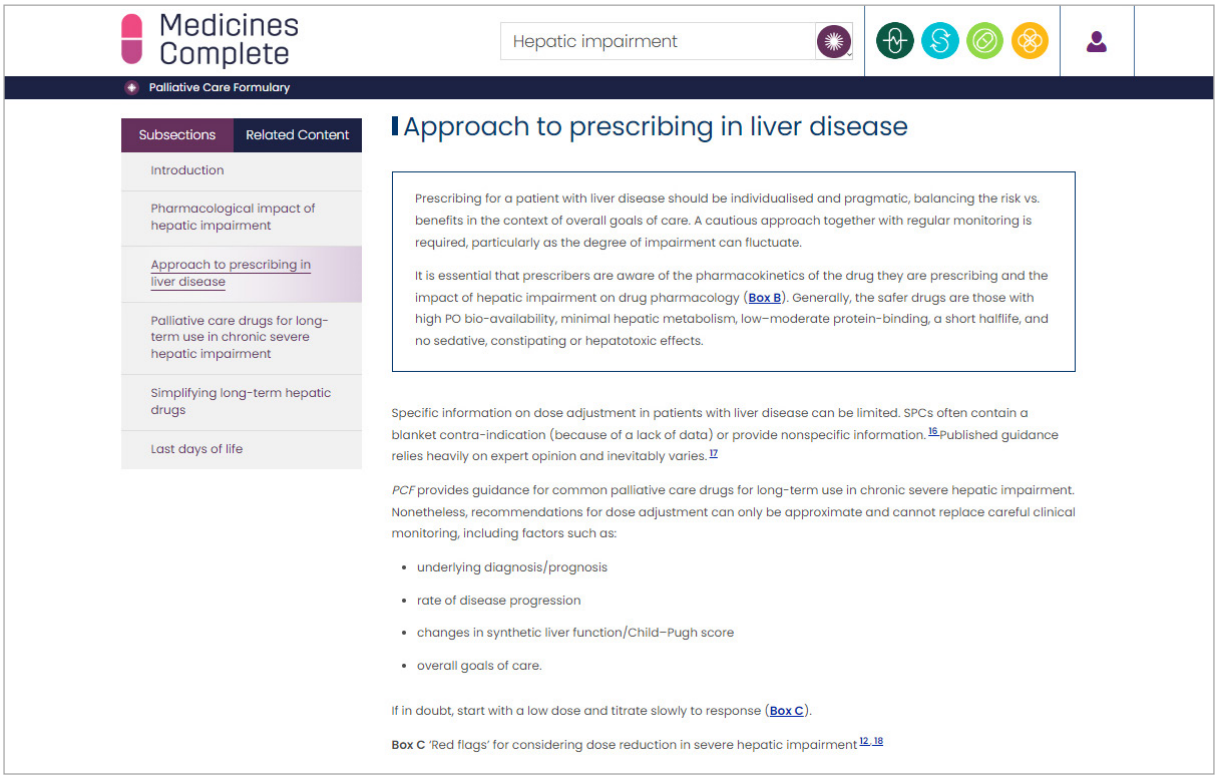
At his first clinic appointment, John is complaining of severe pain and following a full review of his symptoms, the team consider prescribing morphine.

What issues do the team need to consider when prescribing morphine for John?

There is an increased risk of toxicity with all opioids for patients with chronic severe hepatic impairment because of increased opioid receptor sensitivity and reduced integrity of the blood-brain barrier; further their sedative and constipating effects can worsen or sometimes mask hepatic encephalopathy.

The bio-availability and half-life of morphine are significantly increased in patients with chronic severe hepatic impairment. Both the starting dose and frequency of administration should be reduced and titrated slowly. Modified-release products should generally be avoided because of the prolonged duration of action.

PCF Hepatic impairment chapter provides guidance for prescribing drugs commonly used for long-term palliative care symptom relief in patients with chronic severe hepatic impairment with a prognosis of weeks—months or longer, including information on relative safety and specific prescribing advice and doses.



The team decide to start John on a low dose of oral immediate-release morphine.

What counselling points do the team need to discuss with John?

John and his carers should be made aware of the need to obtain urgent medical attention if any signs of toxicity develop, e.g. excessive sedation, respiratory depression or any of the features of worsening hepatic encephalopathy.

John should be warned not to increase the dose without contacting the team and not to drive or use tools or machines if feeling sleepy. He should also be warned that alcohol will have an additive sedative effect and he should avoid taking it.

Because of the risk of opioid-induced constipation, which may add to his risk of hepatic encephalopathy, John should closely monitor his bowel movements to ensure he produces two soft evacuations/day, adjusting his laxative regimen, when needed, within the parameters set by the team.

John should be warned that morphine may initially cause transient nausea lasting up to one week. He should be advised to contact the team to consider an anti-emetic if this becomes intolerable.

One week later, John returns for a clinic review. His mood is quite low, and the team consider whether to prescribe an antidepressant. However, after looking at the risk vs. benefit ratio of the use of antidepressants in chronic severe hepatic impairment, and after further discussion with John they decide to initially offer psychosocial support within the local day care team.

What are the risks of prescribing antidepressants for patients with chronic severe hepatic impairment and what is the antidepressant of choice for this group of patients?

Most antidepressants are significantly hepatically metabolised and highly protein-bound. These factors increase the risk of toxicity in patients with severe hepatic impairment. Several antidepressants cause sedation or constipation which can worsen or mask hepatic encephalopathy.

In palliative care, the first-line choice of antidepressant is generally sertraline or citalopram. Sertraline has very high first-pass metabolism and protein-binding; citalopram less so. Cautious use of low-dose citalopram is probably the best choice for patients with chronic severe hepatic impairment, unless they have additional risk factors for QT prolongation or severe cholestasis. SSRIs decrease platelet aggregation and increase the risk of GI bleeding, and are not a good choice in patients with coagulopathy or oesophageal varices. Additionally, citalopram has a significantly increased half-life in chronic severe hepatic impairment and the time taken to reach steady state and the emergence of undesirable effects may only become apparent after several weeks of regular use.

Nine months later John is admitted as an emergency to the hospice after significant rapid deterioration. A full assessment establishes that John is in the last days of his life and the team want to prescribe anticipatory drugs to ensure timely symptom control as needed.

What drugs are recommended for anticipatory prescribing in patients with end-stage hepatic impairment in the last days of life?

Currently, there are no national guidelines for prescribing in patients with severe or end-stage hepatic impairment in the last days of life. Consensus opinion, based on clinical experience, suggests the use of fentanyl or morphine for pain; fentanyl for breathlessness, with the addition of midazolam when there is concurrent anxiety; midazolam for agitation and restlessness; haloperidol for nausea and vomiting; haloperidol with or without midazolam for delirium; hyoscine butylbromide for noisy rattling breathing.

As most of these drugs have CNS depressant effects and may also cause constipation, one of the major challenges is to alleviate symptoms without precipitating or worsening hepatic encephalopathy. Thus, with all drugs, appropriate caution, close monitoring and individualized titration, initially with small doses, is required. Generally, subcutaneous injections are prescribed on an as needed basis to facilitate this.

PCF Hepatic impairment chapter provides suggested starting doses for drugs for common symptoms in the last days of life for a patient with end-stage hepatic impairment.