

## Guidance for Safety and Dosing of Medicines in Patients With Cirrhosis Is Available

### TO THE EDITOR:

We read with great interest the article by Hayward et al.<sup>(1)</sup> describing medication-related problems (MRPs) in patients with decompensated cirrhosis. They found 375 MRPs among 57 patients randomized to a pharmacist-led intervention. Almost half of these MRPs possessed a high risk of potential harm to the patient and led to a higher rate of unplanned admissions.

The patients included in their study used various medicines in complex regimens.<sup>(1)</sup> The vast majority of these medicines were used for conditions other than the chronic liver disease and were not prescribed by gastroenterologists. We agree with the authors that management and monitoring of patients with cirrhosis is challenging and that physicians may benefit from prescription guidance. We disagree with their statement that a list of potentially inappropriate medicines for decompensated cirrhosis is lacking. While such guidance was absent at the start of their study, we published practical guidance for the safe use of over 200 medicines for patients with cirrhosis in 2018 in a paper that is freely available (<https://www.drugsinlivercirrhosis.org>).<sup>(2)</sup>

This guidance consists of advice on the use of a medicine in patients with cirrhosis (e.g. “can be used” or “avoid the use”) and, if necessary, joined by a dosing recommendation.<sup>(2)</sup> It includes some well-known potentially inappropriate medicines (e.g., nonsteroidal anti-inflammatory drugs). It also includes medicines that have less known inappropriateness in cirrhosis, such as sertraline. Exposure to sertraline is 4 times higher in patients with compensated cirrhosis compared to healthy controls, and exposure is predicted to increase even more in decompensated cirrhosis.<sup>(3)</sup> This endorses that guidance for prescribing is able to assist prescribers managing non-liver-related comorbidities in these patients.

We also studied the potential impact of our guidance in a retrospective real-world study of patients with cirrhosis. Potentially unsafe medications were prescribed in 60% of the 5,618 included patients during follow-up.<sup>(4)</sup> We have not studied the impact of our guidance in a prospective study or on actual patient

outcomes. An interesting approach would be to combine application of our guidance with a medication review, as described by Hayward et al., and examine the effect on hospital admissions and mortality.

In conclusion, tailored pharmacotherapy is needed in cirrhosis, especially in patients with decompensated cirrhosis as they are susceptible to MRPs. Prescribers can be supported by practical guidance on safe prescribing and a high-quality medication review.

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### REFERENCES

- 1) Hayward KL, Patel PJ, Valery PC, Horsfall LU, Li CY, Wright PL, et al. Medication-related problems in outpatients with decompensated cirrhosis: opportunities for harm prevention. *Hepatol Commun* 2019;3:620-631.
- 2) Weersink RA, Bouma M, Burger DM, Drenth J, Harkes-Idzinga SF, Hunfeld N, et al. Evidence-based recommendations to improve the safe use of drugs in patients with liver cirrhosis. *Drug Saf* 2018;41:603-613.
- 3) Démolis J, Angebaud P, Grangé J, Coates P, Funck-Brentano C, Jaillon P. Influence of liver cirrhosis on sertraline pharmacokinetics. *Br J Clin Pharmacol* 1996;42:394-397.
- 4) Weersink RA, Taxis K, Drenth J, Houben E, Metselaar HJ, Borgsteede SD. Prevalence of drug prescriptions and potential safety in patients with cirrhosis: a retrospective real-world study. *Drug Saf* 2019;42:539-546.

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