Treatment for Chronic Hepatitis B

ODPRN

The Ontario Drug Policy Research Network (ODPRN) conducted a drug class review (DCR) on the effectiveness, safety, and accessibility of drugs for the treatment of chronic hepatitis B (CHB) using multiple research methods. **CHB treatments are categorized into two groups of treatments: oral nucleos(t)ides (i.e., adefovir, entecavir, telbivudine, tenofovir, and lamivudine) and injectable interferons (i.e., standard and pegylated).**

What did we find?

EFFICACY + SAFETY

Tenofovir was the most effective treatment for reducing Hepatitis B viral levels, but its overall efficacy is similar to entecavir. Lamivudine was less effective than both tenofovir and entecavir. In 70-80% of patients, resistance to lamivudine develops within 5 years, and patients need to switch to alternative medications, usually tenofovir. Pegylated interferon is also effective for reducing viral levels, but can only be used if the patient has a high viral load and if the liver is functioning well.

There were no significant differences in terms of safety for the various oral drugs. However, patients stopped using lamivudine more often than entecavir because of adverse events. For the injectables, pegylated interferon has significantly more side effects compared with all products and patients also stopped using it more often than entecavir because of adverse events.

ACCESSIBILITY

The current Exceptional Access Program (EAP) process can be an inconvenient and lengthy process for those in urgent situations (i.e., those initiating chemotherapy).

Additionally, CHB is more prevalent in immigrants, with approximately half of all treated patients in Ontario born outside of Canada. Further steps should be taken to ensure that vulnerable populations are not hindered by the process of gaining access to necessary treatments.

COST

Patient affordability was described as having a great influence on CHB treatment selection. Most physicians mentioned that they would prefer to use tenofovir as first-line therapy, but sometimes refrain from doing so because of the high cost of this medication for those without coverage.

The cost effectiveness varies, depending on how healthy/damaged a patient's liver is. Lamivudine was shown to be cost effective in the early stages of disease, before the liver is permanently damaged. Tenofovir was shown to be cost effective for those who have some scarring of the liver but whose liver is still functioning fairly well. Generic entecavir (at 25% of the brand cost) would be cost effective for those who have little or no liver scarring.

What do we recommend?

Lamivudine and entecavir Limited Use and updated EAP criteria to include tenofovir:
Moving lamivudine and entecavir to Limited Use would increase access to treatment for new patients and those in urgent situations (e.g. those initiating chemotherapy). Entecavir was found to be the most cost-effective treatment, if cost reductions to 25% of brand-name could occur.

Further cost-savings could be realized by moving lamivudine to Limited Use. Changes are also recommended to the EAP criteria allowing for earlier access to tenofovir for those in whom entecavir was ineffective or for those unable to tolerate this drug.

Other considerations

1. Evaluate the possible inclusion of pegylated interferon to the EAP as it needs to be administered less frequently than standard interferon.
2. Criteria should be re-visited and updated within 4 years or upon genericization of tenofovir. Pricing negotiations with manufacturers based on pricing reductions (approximately 60%) to allow for cost-effective addition of tenofovir, should also be considered.
3. Evaluate the possible alteration to current EAP process for patients with decompensated cirrhosis to allow for rapid approval via phone.
4. Remove adefovir from the EAP.

How did we conduct our studies?

The ODPRN conducted a drug class review consisting of multiple studies: a qualitative study to determine the experiences of use and prescribing; a systematic review to determine efficacy and safety; a pharmacoepidemiological analysis to determine patterns of use in Ontario and across Canada; an environmental scan to determine national and international guidelines and public drug coverage models; and pharmacoeconomic analyses to determine the cost of public drug funding under different coverage policies. Detailed descriptions of each of these studies are available at the ODPRN website: www.odprn.ca