INAHTA Brief

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Title Drugs for Chronic Hepatitis C Infection

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Reference Canadian Agency for Drugs and Technologies in Health. CADTH therapeutic review. Drugs for chronic hepatitis C infection: clinical review. Ottawa: CADTH; 2016 Jan. (CADTH therapeutic review; vol.3, no.1b). Available from: https://www.cadth.ca/sites/default/files/pdf/TR0008_Clinical_Report-en.pdf
Drugs for chronic hepatitis C infection: cost-effectiveness analysis. Ottawa: CADTH; 2016 Jan. (CADTH therapeutic review; vol.3, no.1c). Available from: https://www.cadth.ca/sites/default/files/pdf/TR0008_Cost-Effectiveness_Report.pdf

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Aim
To assess the comparative efficacy and safety of currently available and emerging regimens for the treatment of chronic hepatitis C (CHC) infection (genotypes 1 to 6), and to assess the comparative cost-effectiveness of regimens for the treatment of CHC infection (genotypes 1 to 4).

Conclusions and Results
Results from the systematic review and indirect treatment comparison suggest that for treatment-naive and treatment-experienced patients with CHC genotype 1 infection, sofosbuvir (SOF) + ledipasvir (LDV); ritonavir-boosted paritaprevir (PAR/RIT) + ombitasvir (OMB) + dasabuvir (DAS) with or without (±) ribavirin (RBV); and daclatasvir (DCV)-based regimens were superior to pegylated interferon plus ribavirin (PR)-based treatments for achieving sustained virologic response (SVR). SOF + LDV and PAR/RIT + OMB + DAS ± RBV were better than DCV-based regimens in some patient subgroups. There was limited evidence for patients with cirrhosis. The data available for genotypes 2 to 4 were limited. For patients with genotype 2 infection, SOF + RBV for 12 weeks significantly improved SVR rates over PR for 24 weeks in treatment-naive patients, but SOF + PR for 12 weeks did not. In treatment-experienced patients, neither SOF + RBV for 16 weeks nor SOF + PR for 12 weeks were significantly different from SOF + RBV for 12 weeks. For patients with CHC genotype 3 infection, SOF + RBV for 24 weeks, DCV + SOF for 12 weeks, and SOF + PR for 12 weeks significantly improved SVR compared with PR for 48 weeks regardless of treatment experience, and there were no significant differences between these regimens. For patients with genotype 4 infection, SOF + PR for 12 weeks and SOF + RBV for 24 weeks significantly improved SVR compared with PR for 48 weeks in treatment-naive patients overall, and SOF + PR for 12 weeks was statistically superior to SOF + RBV for 12 weeks. DCV + asunaprevir + PR for 24 weeks significantly improved SVR compared with SOF + RBV for 12 weeks in treatment-experienced patients overall. There was no statistically significant difference between SOF + RBV for 12 weeks and SOF + RBV for 24 weeks. There was no evidence to allow for inclusion of SOF + PR for 12 weeks in the analysis of treatment-experienced patients with genotype 4 infection. The data for genotype 5 and 6 infection were insufficient for comparative analysis: all six patients with genotype 6 and the single patient with genotype 5 who received SOF + PR for 12 weeks in one study achieved SVR, as did all five patients with genotype 6 infection treated with SOF + PR for 24 weeks in another study.

In terms of safety, among treatment-naive patients, LDV + SOF for 12 weeks, PAR/RIT + OMB + DAS ± RBV for 12 weeks, and DCV-based regimens were associated with significantly lower risks for rash and anemia than PR-based treatments. For rash, PAR/RIT + OMB + DAS + RBV was less favourable than SOF + LDV, PAR/RIT + OMB + DAS without RBV, and DCV-based regimens. For anemia, PAR/RIT + OMB + DAS ± RBV was less favourable than SOF + LDV. For depression, PAR/RIT + OMB + DAS with RBV and DCV-based regimens were less favourable than SOF + LDV. Among treatment-experienced patients, LDV + SOF for 12 weeks, PAR/RIT + OMB + DAS ± RBV for 12 weeks, and DCV-based regimens were associated with significantly less rash and anemia than PR-based treatments, but evidence was limited for depression. For rash, DCV with PR was less favourable than SOF + LDV, PAR/RIT + OMB + DAS, and DCV without PR. For anemia, PAR/RIT + OMB + DAS + RBV was less favourable than SOF + LDV and PAR/RIT + OMB + DAS without RBV.

The pharmacoeconomic analysis suggests that, for each genotype 1 population (treatment-naive non-cirrhotic, treatment-naive cirrhotic, treatment-experienced non-cirrhotic, and treatment-experienced cirrhotic), at least one of the interferon-free therapies appears to be economically attractive compared with PR alone. The drug that is the most cost-effective varies by population, but was generally consistent across fibrosis stages. The economic analysis also suggests that, for genotype 2 CHC infection, of regimens currently approved in Canada, SOF + RBV for 12 weeks was the most cost-effective option for patients who are treatment-naive with cirrhosis and treatment-experienced (regardless of cirrhosis status). The interferon-free or PR-based direct-acting antiviral (DAA) therapies appear not to be economically attractive compared with PR alone in patients with genotype 2 infection who are treatment-naive and non-cirrhotic. For genotype 3 CHC infection, SOF + RBV for 24 weeks was the most cost-effective approved option for patients who are treatment-experienced with or without cirrhosis and patients who are treatment-naive with cirrhosis. The interferon-free or the PR-based DAA therapies did not appear to be economically attractive compared with PR alone for treatment-naive patients with genotype 3 infection without cirrhosis. When including DCV + SOF for 12 weeks into an exploratory analysis, it was the most cost-effective option among the approved regimens for patients with genotype 3 infection without cirrhosis, regardless of previous treatment. For genotype 4 CHC infection, SOF + PR for 12 weeks was the only approved treatment for genotype 4 infection. It was included in an exploratory analysis of treatment-naive, non-cirrhotic patients and was associated with an incremental cost-utility ratio (ICUR) of $63,421 per quality-adjusted life-year (QALY) compared with PR. For patients who are treatment-naive with cirrhosis or those who are treatment-experienced, SOF + RBV for 24 weeks was considered the most cost-effective treatment, but is not currently indicated.

Recommendations
Available in a separate report at:
https://www.cadth.ca/sites/default/files/pdf/TR0008_HepatitisC_RecsReport_e.pdf

Methods
Peer-reviewed literature searches and consultations with experts and stakeholders were used to identify potential prospective studies evaluating currently available and emerging regimens for the treatment of CHC infection (genotypes 1 to 6). Two reviewers independently screened citations, and selected studies according to predefined criteria. Quality assessment of eligible studies was performed by a single reviewer and checked by a second reviewer. Bayesian network meta-analyses were conducted for efficacy and safety outcomes. An economic model was developed in the form of a cost-utility analysis. The primary outcome was the number of QALYs, with treatments compared in terms of the incremental cost per QALY (ICUR).

Further Research or Reviews Required
The following research gaps were identified:

- Lack of head-to-head trials comparing DAA-based regimens with one another
- Sparse evidence for genotypes 5 and 6
- Lack of adequate studies to guide therapy for patients experiencing treatment failure with a DAA-based regimen
- Efficacy and safety of DAA-based regimens for patients with CHC infection and chronic kidney disease, or decompensated liver disease.

Given the rapid, ongoing development of new regimens for CHC infection, it is expected that updated reviews and cost-effectiveness analyses will be required in the near future.

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