Granulocyte colony-stimulating factor for hepatitis C therapy-associated neutropenia: 
systematic review and economic evaluation

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract 
contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the 
reliability of the study and the conclusions drawn.

CRD summary
The objective was to assess the effectiveness and cost-effectiveness of granulocyte colony-stimulating factor for the 
management of neutropenia associated with hepatitis C virus therapy, to avoid reducing the dose of pegylated 
interferon. The authors stated that their findings were inconclusive, because the clinical evidence was weak. The 
methods were robust, which enhances the reliability of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was assess the effectiveness and cost-effectiveness of granulocyte-colony stimulating factor (G-CSF) for 
the management of neutropenia associated with hepatitis C virus (HCV) therapy, to avoid reducing the dose of 
pegylated interferon.

Interventions
The interventions were the addition of G-CSF (filgrastim or pegfilgrastim) versus a dose reduction or discontinuation of 
pegylated interferon. G-CSF was given at a dose of 300 micrograms per week. If the neutropenia was not controlled by 
week three, G-CSF was given twice a week.

Location/setting
Canada/secondary care.

Methods
Analytical approach:
The economic evaluation was based on a decision-tree model, with a lifetime horizon. The authors stated that the 
analysis was carried out from the perspective of the Ministry of Health. Separate analyses were carried out for patients 
with HCV genotype one and those with genotypes two or three.

Effectiveness data:
A systematic search of 20 electronic databases was carried out, with an extensive search of the grey literature. The 
review was performed by two independent reviewers. Wide inclusion criteria were considered and both controlled and 
observational studies were selected. The methodological quality of the included studies was assessed. Only one clinical 
trial was found, and this provided the drug efficacy data. Safety was from several sources, including observational 
studies and case series. The primary outcomes were the sustained virologic response (SVR) and neutrophil count. 
Where multiple sources were available, for inconsistent definitions of neutropenia, the data were synthesised 
qualitatively. Risk ratios or mean values were calculated.

Monetary benefit and utility valuations:
The utility values were estimated, using the Health Utilities Index (HUI).

Measure of benefit:
The summary benefit measures were quality-adjusted life-years (QALYs) and the SVR. A 5% annual discount rate was 
applied.
The economic analysis included the costs of HCV treatment (pegylated interferon and ribavirin), the costs of G-CSF, and the costs of the lifetime treatment of patients whose HCV therapy failed. Other medical costs, such as physician time and laboratory tests, were assumed to be equal for the two arms. The patterns of resource use were from published literature, identified in the review. The treatment strategies for HCV reflected Canadian guidelines. All costs were from available drug catalogues or published studies. They were in Canadian dollars (CAD) and were discounted at an annual rate of 5%. The price year was 2008.

Analysis of uncertainty:
Several one-way sensitivity analyses and analyses of extremes were performed to test if the base-case results were robust.

Results
In patients with genotype one, the costs were CAD 47,416 with G-CSF and CAD 35,535 with dose reduction. The rate of SVR was 0.535 with G-CSF and 0.257 with dose reduction. The QALYs were 2.94 with G-CSF and 1.41 with dose reduction. The incremental cost was CAD 42,737 per additional SVR or CAD 7,785 per QALY gained.

In patients with genotypes two or three, the costs were CAD 20,869 with G-CSF and CAD 16,804 with dose reduction. The rate of SVR was 0.813 with G-CSF and 0.576 with dose reduction. The QALYs were 4.46 with G-CSF and 3.16 with dose reduction. The incremental cost was CAD 17,151 per additional SVR or CAD 3,124 per QALY gained.

The sensitivity analyses found wide confidence intervals around the mean values, but G-CSF generally remained cost-effective at the standard cost per QALY threshold.

Authors' conclusions
The authors stated that their findings were inconclusive, because the clinical evidence was weak. Large well-designed trials were needed.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as G-CSF was an alternative to a reduction in the dose of pegylated interferon, to treat neutropenia in patients with HCV, according to Canadian guidelines. The drug dosage was clearly reported.

Effectiveness/benefits:
A valid approach was used to identify the relevant sources of evidence. The selection process (studies identified and included, and reasons for exclusion) and the methods of synthesis were reported. The design, sample size, and other key characteristics of the selected studies were reported. The quality of these studies was low, including the only randomised controlled trial (RCT) and the prospective studies. Appropriate checklists were used to judge this quality. Both benefit measures were appropriate. They captured the impact of the interventions on a patient's health and QALYs can be compared with the outcomes for other interventions. The utility values for the QALYs were calculated using the HUI, but the sources for these data were not reported.

Costs:
The authors stated that only those costs relevant to the Ministry of Health were analysed. The resource quantities and unit costs were not presented separately and the total costs for only some items were reported. The costs were from published sources identified by the systematic review and it is likely that the most relevant data for Canada were identified. The drug costs were from the manufacturers or drug lists. Some costs were varied in the sensitivity analysis. Details, such as the price year and discount rate, were provided.

Analysis and results:
The results were reported in a table. An incremental analysis was used to synthesise the costs and benefits of the two strategies. A deterministic approach was used to investigate selected areas of uncertainty. The results of the sensitivity analyses were reported in a table. The authors noted that the main limitation of their analysis was the poor quality of the
clinical sources that did not allow consistent conclusions to be drawn on the efficacy of G-CSF; only one trial, with a small sample, was identified. The results were similar to those of another published economic evaluation and might be transferable to similar settings.

Concluding remarks:
The methods were robust, which enhances the reliability of the authors’ conclusions.

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