Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Faldaprevir for treating genotype 1 chronic hepatitis C

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of faldaprevir within its licensed indication for treating genotype 1 chronic hepatitis C.

Background

The hepatitis C virus (HCV) causes inflammation of the liver and affects the liver's ability to function. HCV is a blood-borne virus, meaning that it is spread by exposure to contaminated blood. Infected needles used for injecting drugs are currently the most common route of transmission. Symptoms of chronic hepatitis C are typically mild and non-specific, including fatigue, flu-like symptoms, anorexia, depression, sleep disturbance, pain, itching and nausea. Often, people with hepatitis C do not have any symptoms, and 15 to 20% of infected people naturally clear their infections within 6 months. However, the remainder develop chronic hepatitis which can be life-long.

Chronic hepatitis C is categorised according to the extent of liver damage, as mild, moderate, or severe (where severe refers to cirrhosis). About 30% of people infected with chronic hepatitis C will develop cirrhosis; the time for progression to cirrhosis varies, but takes 40 years on average. Cirrhosis can progress to become 'decompensated', where the remaining liver can no longer compensate for the loss of function. Liver transplantation may be needed for people with decompensated cirrhosis.

The true incidence of chronic hepatitis C is difficult to establish and likely to be underestimated because many people do not have symptoms. There are 6 major genotypes and several subtypes of HCV, the prevalence of each vary geographically. People can be infected with more than one genotype. The most recent national estimates (2012) suggest that around 216,000 individuals are chronically infected with HCV in the UK. However, about 5 out of every 6 people with chronic hepatitis C are unaware of their infection.

The aim of treatment is to prevent liver disease progression, hepatocellular carcinoma development, and HCV transmission. Treatment options depend on HCV genotype. For those with mild HCV, a 'watchful waiting' approach may be agreed, on an individual basis, between the patient and clinician. NICE technology appraisals 75 and 106 recommend that standard treatment for the majority of people with chronic hepatitis C, regardless of disease severity, is combination therapy with ribavirin and either peginterferon alfa-2a or peginterferon alfa-2b. Monotherapy with peginterferon alfa-2a or peginterferon alfa-2b is recommended for patients who are unable to tolerate

ribavirin or for whom ribavirin is contraindicated. NICE technology appraisal 200 recommends that people who have been previously treated with peginterferon alfa and ribavirin or with peginterferon alfa monotherapy have an option to receive further courses of peginterferon alfa and ribavirin. Shortened courses of combination therapy are also recommended as an option for certain patient subgroups.

For people with genotype 1 chronic hepatitis C with compensated liver disease, who have or have not been previously treated, NICE guidance also recommends telaprevir in combination with peginterferon alfa and ribavirin (TA252) or boceprevir in combination with peginterferon alfa and ribavirin (TA253).

The technology

Faldaprevir (brand name unknown, Boehringer Ingelheim) is an inhibitor of the NS3/4A serine protease of the hepatitis C virus which prevents viral replication. It is orally administered.

Faldaprevir in combination with peginterferon alfa and ribavirin does not currently have a UK marketing authorisation for the treatment of chronic hepatitis C. It has been studied in combination with peginterferon alfa and ribavirin in clinical trials in people with genotype 1 chronic hepatitis C (with and without HIV) who have and have not received previous treatment, compared with placebo. Faldaprevir in combination with peginterferon alfa-2a and ribavirin has also been compared with telaprevir for treating genotype 1 chronic hepatitis C in people who have had previous treatment with peginterferon alfa and ribavirin.

Intervention(s)	Faldaprevir in combination with peginterferon alfa and ribavirin
Population(s)	Adults with genotype 1 chronic hepatitis C • who have not been previously treated • in whom previous treatment with peginterferon alfa and ribavirin has been ineffective
Comparators	• Peginterferon alfa and ribavirin • Telaprevir in combination with peginterferon alfa and ribavirin • Boceprevir in combination with peginterferon alfa and ribavirin

Outcomes	The outcome measures to be considered include: • sustained virological response • degree of virological response • mortality • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If evidence allows the following subgroup will be considered: • Co-infection with HIV Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations and NICE pathways	Related Technology Appraisals: Technology appraisal No. 253, Apr 2012, 'Boceprevir for the treatment of genotype 1 chronic hepatitis C'. Review Proposal Date Apr 2015. Technology appraisal No. 252, Apr 2012, 'Telaprevir for the treatment of genotype 1 chronic hepatitis C'. Review Proposal Date Apr 2015. Technology appraisal No. 200, Sep 2010, 'Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C'. Review Proposal Date Sep 2013. Technology appraisal No. 106, Aug 2006, 'Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C' (partially updated in TA200). Review Proposal Date Sep 2013. Technology appraisal No. 75, Jan 2004, 'Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C' (partially updated in TA200). Review Proposal Date Sep 2013. Proposed technology appraisal, 'Sofosbuvir for treating chronic hepatitis C'. Publication TBC. Proposed technology appraisal, 'Simeprevir for treating genotype 1 and 4 chronic hepatitis C'. Publication TBC. Related Guidelines: Clinical Guideline in Preparation, 'Hepatitis C'. Earliest anticipated date of publication TBC. Related Public Health Guidance/Guidelines: Public Health Guidance No. 18, Feb 2009, 'Needle and syringe programmes'.
Related NHS England Policy	None.

Questions for consultation

Have all relevant comparators for faldaprevir in combination with peginterferon alfa and ribavirin been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for genotype 1 chronic hepatitis C?
- Should the sequence of treatments be considered?

Is the subgroup suggested in 'other considerations appropriate? Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which faldaprevir in combination with peginterferon alfa and ribavirin will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)

Subject to referral by the Department of Health, the invite for participation in this technology appraisal is anticipated for after January 2014, when new arrangements for the pricing of pharmaceuticals are expected to be in place. Consequences for this appraisal will be explored through further consultation on the scope pre-invitation.