# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal

## Grazoprevir–elbasvir for treating chronic hepatitis C

## Final scope

### Remit/appraisal objective

To appraise the clinical and cost effectiveness of grazoprevir–elbasvir within its marketing authorisation for treating 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 infected blood. Contaminated needles used to inject drugs are currently the most common route of HCV 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 approximately 20% of infected people naturally clear their infections within 6 months[1]. However, the remainder develop chronic hepatitis C 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 20% of people with chronic hepatitis C will develop cirrhosis[2]; the time for progression to cirrhosis varies, but takes 20-30 years on average[2]. Cirrhosis can progress to become 'decompensated', where the remaining liver can no longer compensate for the loss of function. A small percentage of people with chronic hepatitis and cirrhosis also develop hepatocellular carcinoma. Liver transplantation may be needed for people with decompensated cirrhosis or hepatocellular carcinoma.

The true prevalence of HCV infection is difficult to establish and likely to be underestimated because many people do not have symptoms. As a result a significant number of people remain undiagnosed. There are 6 major genotypes and several subtypes of HCV; the prevalence of each varies geographically. Recent estimates (2012) suggest that around 160,000 people are chronically infected with HCV in England[4], and that approximately 90% of these people are infected with genotype 1 or genotype 3[4].

The aim of treatment is to cure the HCV infection, and prevent liver disease progression, hepatocellular carcinoma development, and HCV transmission. The HCV genotype influences treatment decisions and response. For those with mild hepatitis C, a 'watchful waiting' approach may be agreed between the patient and clinician on an individual basis. NICE guidance on hepatitis C (NICE technology appraisal guidance 75, 106, 200, 252, 253, 330, 331, 363, 364 and 365) recommend:

- combination therapy with ribavirin and either peginterferon alfa-2a or peginterferon alfa-2b for people with chronic hepatitis C regardless of disease severity, genotype or treatment experience.
- monotherapy with peginterferon alfa-2a or peginterferon alfa-2b is recommended for people who are unable to tolerate ribavirin or for whom ribavirin is contraindicated.
- telaprevir in combination with peginterferon alfa and ribavirin for people with genotype 1 chronic hepatitis C.
- boceprevir in combination with peginterferon alfa and ribavirin for people with genotype 1 chronic hepatitis C.
- sofosbuvir in combination with ribavirin, with or without peginterferon alfa, as an option for specific people with genotypes 1–6 chronic hepatitis C.
- simeprevir in combination with peginterferon alfa and ribavirin as an option for people with genotype 1 or 4 chronic hepatitis C
- ledipasvir–sofosbuvir as an option for specific people with genotype 1 or 4 chronic hepatitis C
- daclatasvir in combination with sofosbuvir, with or without ribavirin, as an option for specific people with genotype 1, 3 or 4 chronic hepatitis C
- daclatasvir in combination with peginterferon alfa and ribavirin, as an option for specific people with genotype 4 chronic hepatitis C
- ombitasvir–paritaprevir–ritonavir with or without dasabuvir or ribavirin as an option for genotype 1 or 4 chronic hepatitis C.

**The technology**

Grazoprevir–elbasvir (brand name unknown, Merck Sharp & Dohme) disrupts the biogenesis of components necessary for HCV replication by inhibiting key HCV proteins. It is orally administered as a fixed-dose combination product.

Grazoprevir–elbasvir does not currently have a marketing authorisation in the UK for treating chronic hepatitis C. It has been studied in clinical trials as monotherapy and in combination with ribavirin or sofosbuvir in adults with genotype 1–6 HCV.

| **Intervention(s)** | Grazoprevir–elbasvir |
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<table>
<tr><td>Population(s)</td><td>People with chronic hepatitis C:<ul><li>who have not had treatment for chronic hepatitis C (treatment-naive)</li><li>who have had treatment for chronic hepatitis C (treatment-experienced)</li></ul></td></tr>
<tr><td>Comparators</td><td><ul><li>best supportive care (watchful waiting) (genotypes 1-6)</li><li>boceprevir in combination with peginterferon alfa and ribavirin (for genotype 1 only)</li><li>daclatasvir in combination with peginterferon alfa and ribavirin (for specific people with genotype 4; as recommended by NICE)</li><li>daclatasvir in combination with sofosbuvir, with or without ribavirin (for specific people with genotype 1, 3 or 4; as recommended by NICE)</li><li>ledipasvir–sofosbuvir (for specific people with genotype 1 or 4; as recommended by NICE)</li><li>ombitasvir–paritaprevir–ritonavir with or without dasabuvir or ribavirin (for genotype 1 or 4)</li><li>peginterferon alfa with ribavirin (for genotypes 1-6)</li><li>simeprevir in combination with peginterferon alfa and ribavirin (for genotype 1 or 4)</li><li>sofosbuvir in combination with ribavirin, with or without peginterferon alfa (for specific people with genotypes 1-6; as recommended by NICE)</li><li>telaprevir in combination with peginterferon alfa and ribavirin (for genotype 1 only)</li></ul></td></tr>
<tr><td>Outcomes</td><td>The outcome measures to be considered include:<ul><li>sustained virological response</li><li>development of resistance to grazoprevir–elbasvir</li><li>mortality</li><li>adverse effects of treatment</li><li>health-related quality of life.</li></ul></td></tr>
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| **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.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | If evidence allows the following subgroups will be considered:<br>• genotype<br>• people with renal impairment<br>• co-infection with HIV<br>• people with and without cirrhosis<br>• people with advanced liver disease<br>• post-liver transplantation<br>• people with haemoglobinopathies (for example, sickle cell disease, thalassaemia major)<br>• response to previous treatment (non-response, partial response, relapsed)<br>• people who are intolerant to or ineligible for interferon treatment<br><br>If evidence allows the impact of treatment on reduced onward HCV transmission will also be considered.<br><br>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br><br>‘Ombitasvir–paritaprevir–ritonavir with or without dasabuvir for treating chronic hepatitis C’ (2015). NICE Technology Appraisal 365.<br><br>‘Daclatasvir for treating chronic hepatitis C’ (2015). NICE Technology Appraisal 364.<br><br>‘Ledipasvir–sofosbuvir for treating chronic hepatitis C’ |

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| | (2015). NICE Technology Appraisal 363.<br>'Simeprevir for treating genotype 1 or 4 chronic hepatitis C' (2015). NICE Technology Appraisal 331. Review date February 2016.<br>'Sofosbuvir for treating chronic hepatitis C' (2015). NICE Technology Appraisal 330. Review date February 2016.<br>'Boceprevir for the treatment of genotype 1 chronic hepatitis C' (2012). NICE Technology Appraisal 253. Review Date April 2015.<br>'Telaprevir for the treatment of genotype 1 chronic hepatitis C' (2012). NICE Technology Appraisal 252. Review Date April 2015.<br>'Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C' (2010). NICE Technology Appraisal 200. Guidance added to static list December 2013.<br>'Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C (partially updated in TA200)' (2006). NICE Technology Appraisal 106. Guidance added to static list December 2013.<br>'Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C (partially updated in TA200)' (2004). NICE Technology Appraisal 75. Guidance added to static list December 2013.<br>Related Guidelines:<br>'Hepatitis C: Diagnosis and management of hepatitis C'. NICE Clinical Guideline. Publication date to be confirmed.<br>Related Public Health Guidance:<br>'Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection' (2012). NICE Public Health Guidance 43.<br>Related NICE Pathways:<br>'Hepatitis B and C' (2012). NICE pathway.<br>http://pathways.nice.org.uk/pathways/hepatitis-b-and-c-testing |

| Related National Policy | Clinical Commissioning Policy Statement: Treatment of chronic Hepatitis C in patients with cirrhosis:<br>http://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/06/hep-c-cirrhosis-polcy-statmnt-0615.pdf<br>NHS England Manual for prescribed specialised services 2013/2014. Sections 16 and 65:<br>http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf<br>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 2–4. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf |
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## References


1. Hepatitis C Trust (2014). About hepatitis C. Accessed April 2015. Available at: http://www.hepctrust.org.uk/about-hepatitis-c

2. World Health Organisation (2015). Hepatitis C. Accessed April 2015. Available at: http://www.who.int/csr/disease/hepatitis/Hepc.pdf?ua=1

3. Department of Health (2004). Hepatitis C: Essential information for professionals and guidance on testing. Accessed April 2015. Available at: http://www.nhs.uk/hepatitisc/SiteCollectionDocuments/pdf/essential-information-for-professionals-and-guidance-on-testing.pdf

4. Public Health England (2014). Hepatitis C in the UK: 2014 report. Accessed April 2015. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/337115/HCV_in_the_UK_2014_24_July.pdf