

**Interim Clinical Commissioning  
Policy Statement:**

**Sofosbuvir + Daclatasvir/Ledipasvir  
+/- Ribivirin for defined patients with  
Hepatitis C**

**April 2014**

**Reference: NHS ENGLAND A02/PS/b**



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<b>Document Purpose</b>	Guidance
<b>Document Name</b>	Sofosbuvir + Daclatasvir/Ledipasvir +/- Ribivirin for defined patients with Hepatitis C (A02/PS/b)
<b>Author</b>	NHS England
<b>Publication Date</b>	19 April 2014
<b>Target Audience</b>	Foundation Trust CEs , Medical Directors, Directors of PH, NHS England Regional Directors, NHS England Area Directors, NHS Trust Board Chairs, Directors of Finance, Communications Leads, NHS Trust CEs
<b>Additional Circulation List</b>	CCG Clinical Leaders, CCG Chief Officers, CSO Managing Directors, GPs
<b>Description</b>	NHS England will commission Sofosbuvir + Daclatasvir/Ledipasvir +/- Ribivirin for the treatment of Hepatitis C in adults in accordance with the criteria outlined in this document. This policy outlines the arrangements for funding of this treatment for the population in England.
<b>Cross Reference</b>	None
<b>Superseded Docs</b> (if applicable)	N/A
<b>Action Required</b>	
<b>Timing / Deadlines</b> (if applicable)	
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### Document Status

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# NHS England

## **Clinical Commissioning Policy Statement: Sofosbuvir + Daclatasvir/Ledipasvir +/- Ribivirin for defined patients with Hepatitis C**

First published: April 2014

**Prepared by NHS England Clinical Reference Groups for Infectious Diseases  
and Hepato-pancreas biliary**

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<b>POLICY STATEMENT:</b> <b>Sofosbuvir + Daclatasvir/  Ledipasvir +/- Ribivirin for  defined patients with  Hepatitis C</b>	<b>Policy Ref:</b> <b>NHS England A02/PS/b</b>
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<b>Background:</b>	<p>Chronic infection with the hepatitis C virus causes cirrhosis and liver cancer in a significant proportion of patients. Once cirrhosis has developed, hepatic decompensation and other potentially fatal complications occur and liver transplantation is required. Viral eradication prevents disease progression but, until recently, successful therapy has not been possible in patients with advanced disease, as the current drugs are poorly tolerated and have low efficacy at this stage. The development of new direct acting antiviral (DAA) drugs provides effective, orally given, antiviral regimens which offer the potential for curative therapy in all patients with hepatitis C, including those patients with advanced cirrhosis.</p> <p>The first DAA drug with potential in these patients – Sofosbuvir – has recently been licensed in Europe and will be reviewed by NICE during 2014. This policy statement describes interim criteria to operate prior to the publication of the NICE Technology Appraisal, and anticipated NICE directed access, for a cohort of patients with advanced disease who are likely to develop serious complications whilst awaiting such approval.</p>
<b>Commissioning position:</b>	<p>NHS England will as an interim position commission Sofosbuvir for adults within the defined cohort of patients with hepatitis C in accordance with the criteria outlined in this document. This treatment will need to be given in combination with other DAA's (specifically daclatasvir or ledipasvir – obtainable via compassionate use programmes) as part of this interim policy.</p> <p>Patients eligible for treatment are those with significant risk of death or irreversible damage within the next 12 months, irrespective of genotype. For example, there are patients' listed for liver transplantation and others who are either approaching but not yet on a liver transplant waiting list, or who may not fulfil other criteria to allow liver transplantation to be performed.</p> <p>Such patients would be defined as follows:</p> <ol style="list-style-type: none"> <li>1) Evidence of present or previous decompensated</li> </ol>

	<p>cirrhosis with an episode of ascites, variceal bleeding, or encephalopathy.</p> <p>2) Child Pugh Score <math>&gt;</math> or <math>=</math> 7</p> <p>3) Non-hepatic manifestation of HCV infection likely to lead to irreversible damage within 12 months AND intolerant of or failed to respond to pegylated interferon-based treatment.</p> <p>4) Exceptional cases: Only patients at high risk of death, needing a liver transplant, or likely to suffer irreversible harm in the next 12 months, who are not suitable for treatment with pegylated interferon-based treatment, will be eligible.</p> <p>The scheme will treat ~500 patients who fulfil the criteria for a total treatment duration of 12 weeks.</p> <p>Treatment will be delivered through specialised centres (circa 15) that will be selected for this role and which can meet the stated criteria and offer reasonable geographic access.</p> <p>In creating this policy statement NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of these treatments in current clinical practice, whether scientific research has shown the treatments to be of benefit to patients (including how any benefit is balanced against possible risks), and whether its use represents the best use of NHS resources.</p>
<b>Effective from:</b>	<b>April 2014</b>
<b>Evidence summary:</b>	<p>Sofosbuvir has proven to be very effective and well tolerated in combination with pegylated interferon and ribavirin in most subgroups of patients with chronic hepatitis C, including those with cirrhosis. However it is known that those with severe cirrhosis tolerate pegylated interferon very poorly, with a significant chance of treatment-induced liver decompensation. Emerging data which has been reviewed by the CRGs' subgroup (which is drawn from recent presentations at AASLD and EASL) show that sofosbuvir is safe and effective even in advanced, decompensated cirrhosis and restores liver function in a high proportion of cases.</p> <p>Of particular note is that Sofosbuvir has robust data supporting its high efficacy and good tolerability when combined with other agents in interferon-free regimens, including those with significant cirrhosis. Sofosbuvir and ribavirin has shown good efficacy and safety, but may be required for 24 weeks. Combining Sofosbuvir and ribavirin</p>

	<p>with either Daclatasvir or Ledipasvir (NS5A Direct Acting Antivirals) has demonstrated high efficacy and good tolerability and safety in 12 week oral only regimens. These NS5A DAAs are in phase 3 development and are to be available, cost-free, for compassionate use in combination with Sofosbuvir. Such Sofosbuvir, ribavirin and NS5A combinations are recommended for use in such patients by the European Medicines Agency.</p> <p>Early access to DAA combinations prior to NICE recommendation offers the chance to cure a cohort of HCV infection patients who may otherwise die or progress to liver transplantation. Treatment of such patients will reduce mortality and may prevent the need for liver transplantation. Even if liver transplantation is still required for some treated patients, prior virological cure prevents HCV recurrence which results in significant associated morbidity and mortality, thereby maximising use of scarce organs and directly benefitting patients. Such pre-transplantation treatment is evidence-based.</p> <p>Cost Effectiveness: The NHS list price for Sofosbuvir is £34,983 per patient with an additional estimated £2,400 for ribivirin required for the full course of treatment (this is a lower cost than currently incurred with other agents).</p> <p>This is less than the cost will be post a positive NICE TA publication when the required combination drugs will no longer be free of charge.</p> <p>The costs of early treatment will be incurred anyway but at a later date for most patients as it is anticipated NICE will consider its use cost effective based on the cost effectiveness modelling used to support this policy statement.</p> <p>In addition the cost of early treatment for the proposed cohort will be offset against other high cost treatments, including</p> <ul style="list-style-type: none"> <li>a) for some patients a reduced need for liver transplants (c.£50K per case avoided)</li> <li>b) for others who are not eligible for transplant (c30k over 3 years)</li> <li>c) reduced complications post-transplant and avoidance of related expensive treatment of cirrhosis.</li> <li>d) reduced expenditure on therapies for liver cancer</li> <li>e) the imminent availability of sofosbuvir is likely to reduce prescriptions for alternative oral anti-viral agents, such as telaprevir and boceprevir</li> </ul> <p>A cost effectiveness calculation completed by Gilead and</p>
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	reviewed by the CRG sub-group indicates that with a very conservative response to therapy of 40% (i.e. 40% of patients respond to therapy and do not progress) the ICER using the standard modelling approach adopted by NICE is £3,965. i.e highly cost-effective. With a more realistic response rate of 70% the ICER is dominant and the approach is extremely good value for money.
<b>Equality impact:</b>	Throughout the production of this document, due regard has been given to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited in under the Equality Act 2010) and those who do not share it.
<b>Responsible CRG:</b>	Infectious Diseases & Hepato-Pancreas-Biliary Clinical Reference Groups
<b>Mechanism for Funding:</b>	Through NHS England standard contract arrangements
<b>Date Approved</b>	16 April 2014
<b>Policy review date:</b>	This is an interim policy statement and will be reviewed in line with the NICE TA timeframe and no later than 31st March 2015

## References

Berenguer M. Natural history of recurrent hepatitis C. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society 2002;8:S14-18.

Carrion JA et al. Antiviral therapy increases the risk of bacterial infections in HCV-infected cirrhotic patients awaiting liver transplantation: A retrospective study. Journal of hepatology 2009;50:719-728.

Forns X et al. Initial Evaluation of the Sofosbuvir Compassionate Use Program for Patients With Severe Recurrent HCV Following Liver Transplantation. 64th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD 2013). Washington, DC. November 1-5, 2013.

MP Curry XF et al. Pretransplant Sofosbuvir and Ribavirin to Prevent Recurrence of HCV Infection after Liver Transplantation. 64th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD 2013). Washington, DC. November 1-5, 2013

Jacobson IM et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368(20):1867-77.

Lawitz E et al. Sofosbuvir for previously untreated chronic hepatitis C infection. *N Engl J Med*. 2013;368:1878-87.

Zeuzem S al. Sofosbuvir + Ribavirin for 12 or 24 Weeks for Patients With HCV Genotype 2 or 3: the VALENCE Trial. *The Liver Meeting® 2013: 64th Annual Meeting of the American Association for the Study of Liver Diseases*, Washington, DC. November 1-5, 2013.

Crespo G MZ, Navasa M, Forns X. Viral hepatitis in liver transplantation. *Gastroenterology* 2012;142:1373-1383.

Everson GT et al. Efficacy of an Interferon- and Ribavirin-Free Regimen of Daclatasvir, Asunaprevir, and BMS-791325 in Treatment-Naive Patients With HCV Genotype 1 Infection. *Gastroenterology*. 2013 Oct 30. pii: S0016-5085(13)

Sulkowski MS et al. High rate of sustained virologic response with the all-oral combination of daclatasvir (NS5A Inhibitor) plus sofosbuvir (nucleotide NS5B inhibitor), with or without ribavirin, in treatment-naive patients chronically infected with HCV genotype 1, 2, or 3. *63rd Annual Meeting of the American Association for the Study of Liver Disease*, Boston, 2012.

Fontana RJ et al. Sofosbuvir and daclatasvir combination therapy in a liver transplant recipient with severe recurrent cholestatic hepatitis C. *Am J Transplant*. 2013 Jun;13:1601-5.

Sulkowski et al Sustained Virologic Response With Daclatasvir Plus Sofosbuvir ± Ribavirin (RBV) in Chronic HCV Genotype (GT) 1-Infected Patients Who Previously Failed Telaprevir (TVR) or Boceprevir (BOC) *EASL 48th Annual Meeting April 24th - 28th 2013 The Netherlands, Amsterdam*