NICE appraisal of sofosbuvir for treating chronic hepatitis C

Consideration of the case for extending the period before funding needs to be made available for a NICE technology appraisal

Background

1. Under Regulations[1] made under the Health and Social Care Act 2013, NICE is required to specify, in the guidance that results from a technology appraisal, the period within which the funding necessary to enable its recommendations to be applied must be made available (the 'deferred funding period').

2. This deferred funding period is 3 months unless one of the following conditions applies:

    a. The health technology cannot be appropriately administered until training is in place;

    b. The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place;

    c. The health technology cannot be appropriately administered until other appropriate health services resources, including staff, are in place;

    d. The health technology is not yet available in England.

3. NICE has completed its appraisal of sofusbuvir, which has a marketing authorisation for the treatment of chronic hepatitis C, in combination with other medicines. The Final Appraisal Determination will be released to consultees, for appeal, in December. It recommends the use of sofosbuvir in specified circumstances (Appendix A).

4. The text in italics is taken from the letters to NICE from NHS England (Appendix B).

Request to vary the deferred funding period from NHS England

5. NICE has received a request from NHS England (Appendix 2) to extend the deferred funding period. The request has been made in the context of a likely significant demand for treatment, and the knowledge that a number of other treatments, currently being appraised by NICE, may become available during 2015. NHS England has confirmed that the treatment of hepatitis C is a

[1] 'The National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013'

priority and notes that 'the *most recent national estimates suggest that around 160,000 adults are chronically infected with hepatitis C (HCV) in England in 2012. Current numbers of patients treated are estimated at 5,000 per year in England - 3% of those currently infected but this will increase rapidly. The CRG (Clinical Reference Group) Hepatitis C sub group have estimated that 10-15,000 people per year may come forward seeking HCV treatment'.*

6. NHS England considers that it needs more time than the standard 3 month period allows in order to put in place the resources and arrangements necessary to enable it to effectively implement the recommendations in the appraisal.

7. NHS England considers that the arrangements for the care of people living with hepatitis C are complex, involving *'many components of care delivery in different health settings. Commissioners involved in the diagnostic and treatment hepatitis C pathway include 'NHS England Specialised services, Health and Justice, Public Health England, Local Authorities and Clinical Commissioning Groups and Primary Care.'* It considers that the availability of sofosbuvir, and the potential for other treatments to follow, will challenge these arrangements and so it wishes to establish a 'task and finish group' to *'bring together those involved in commissioning services involved in the Hepatitis C pathway to clarify responsibilities and to agree a coherent set of priorities'.* It anticipates that this group will complete its work by the end of March 2015 and that the actions which arise from it will be implemented in the 2015/16 financial year.

8. NHS England intends to commission a series of *'Hepatitis C Networks'*, consisting of specialist centres which will each manage a caseload of patients, working in partnership with other providers of care in the NHS and in the justice system. The initiative would provide a centralised resource for patients whose care '*occurs as an adjunct to the delivery of other services including HIV, drug and alcohol, sexual health and prison health services, as well as from within gastroenterology and specialist hepatology services'.* Each centre will have a multi-disciplinary care (MDT) team which *will 'support selection of the optimal treatment regimen for each patient.* NHS England estimates that it will take 9 months to establish these centres, with the process allowing for candidates to build partnerships with NHS, local government and prison health services.

9. NHS England also intends to establish a database to 'support development of a national database of treatment and collection of outcomes to inform future treatment and commissioning of clinically effective care. It argues that the slow development of liver diseases means that some patients don't need immediate treatment, on clinical grounds, but that any decision to delay treatment would need to be supported by *'robust surveillance and recall*

systems which are not yet in place'. It says that *'a national Dashboard is already being developed for 2015/16 that will provide evidence of the reduction in harm from increased treatment of hepatitis C'* but gives no other information about how long it might take to fully implement its plans.

10. NHS England argues that *'historic low uptake of both testing and treatment means that providers have stated they would need to increase staff resources particularly specialist pharmacy and nurse specialist support in order to treat the expected increase in demand'.* No indication of the number of staff involved has been provided, although they appear to be associated with the proposed network centres.

11. NHS England concludes its case for a variation to the deferred funding period by stating that it *'believes that the introduction of new Hepatitis C treatments will fundamentally change how we treat those affected. However, in order to ensure that the services we provide are both fit for purpose and can deliver these new treatments that ensure best outcomes for our patients we feel it is imperative that we are given sufficient time to implement the strategy outlined above before we are required to fund drugs that may be used inappropriately and to ensure systems are in place to collect outcomes data to inform future.*

12. NHS England has confirmed that it will continue to approve the use of sofosbuvir for those in immediate and urgent need of treatment during the deferred funding period. This will happen under the terms of the interim commissioning policy which is currently in place.[2]

Consideration of the request

13. NHS England has set out 4 principal reasons why it considers a variation to the deferred funding period is justified:

    a. The need to complete the work of the 'task and finish' service redesign group.

    b. A substantial demand for treatment with sofosbuvir, which it anticipates will increase further, as patients who have not sought active treatment in the past will come forward, and which will be increased further by new patients identified through public awareness campaigns and screening of high risk groups, which have either been initiated or which are planned.

    c. The need to establish a Hepatitis C Network, which will involve setting up a series of centres with the staff and the other resources and

[2] Interim Clinical Commissioning Policy Statement: sofosbuvir + daclatasvir/ledipasvir +/- ribivirin for defined patients with Hepatitis C. NHS England

systems necessary to provide a multi-disciplinary team approach to care.

d. The establishment of a national database and dashboard to monitor and support individual care.

14. NHS England does not refer to the incremental budget impact of treating patients with sofosbuvir. Estimates of this vary because it is not clear how many patients will come forward for treatment. In addition, although it cannot be a specific consideration in this decision, the widening of treatment options, should forthcoming appraisals of other new treatments for hepatitis C have positive outcomes, will lead to increasing numbers of patients seeking and receiving treatment.

15. NHS England is clearly concerned about its ability to make sofosbuvir available in the way it considers necessary for planned, efficient and properly audited care. It has advised NICE that *'an end date of August 2015 fits in with (our) timescales to support implementation'*.

16. In considering the argument for establishing the Network, NHS England say that they intend to *'… test some of the assumptions on the long term cost effectiveness of treatment and the impact this has on current costs in the acute sector of treating Hepatitis related liver failure'.* NICE does not agree that any further analysis of the cost effectiveness of the use of sofosbuvir is required and its consideration of the case for extending the deferred funding period takes no account of it.

17. The argument for a delay, based on the need to establish a national database and dashboard is not supported by a timescale. In addition, it appears that the dashboard component is, in any event, already being put in place. The consequences of not having the database at the same time as the dashboard are not made clear.

18. The work of the task and finish group is likely to be completed within the normal deferred funding period.

19. NHS England's case for an extension to the deferred funding period therefore needs to be considered against criteria b) and c) as set out in paragraph 2, above. It is clear that criterion d), the non-availability of the technology, does not apply. It is possible that criterion a), relating to the need to provide training, may also apply to staff working the proposed Network centres. However, the substance of the case for delay appears to relate to the organisational and staffing arrangements for the Network.

20. The question as to whether an extension to the deferred funding period is warranted appears to turn on whether either, or a combination of a substantial

volume of patients seeking access to sofosbuvir, and the need to establish the Hepatitis C Network (with or without the database and monitoring function) amount to a substantive argument. Patients who consider that they can benefit from treatment now, supported as they may well be by their clinicians, may not wish to wait for treatment even though they may recognise the benefits of their care being part of a nationally-networked service. NHS England, on the other hand, will argue that it has a responsibility to manage its resources efficiently in the interests of both current and future patients.

21. It is clear that sofosbuvir marks a step change in the treatment available to patients with hepatitis C. NICE has recommended its use, with some restrictions because it is clinically and cost effective. Having done so, the Institute should be cautious about introducing any delay in patients gaining access to treatments from which they may benefit. However, it should also avoid placing the NHS in a position of confronting a significant tide of expectation from patients for access to care which they do not feel equipped to provide. That would risk sub-optimal treatment decisions and may place current service provision under an inappropriate level of stress.

22. The responsibility for securing care for the NHS in England rests with NHS England. NICE should be cautious and sure of its judgement before requiring NHS England to provide services that it does not consider that it can provide, or provide safely and efficiently. In effect, NICE would have to conclude that NHS England was mistaken. NHS England has indicated that it does not currently have in place the arrangements that it considers necessary for sofosbuvir to be provided. Its position, in setting out what it believes it needs to do to put the necessary arrangements in place, has credibility. NICE should be wary of substituting its judgement for NHS England's in this respect and so it therefore proposes to grant an extension to the deferred funding period until 31 July 2015, under criteria b) and c) in paragraph 2 above.

Consultation

23. Under the Regulations, NICE is required to consult on the appropriate period that may be specified in a technology appraisal recommendation and that consultation must include the Secretary of State and the Board.

24. In order to minimise further delay in implementing the guidance, the consultation period on this proposal to extend the deferred funding period will run until Thursday 11 December at 5pm.

25. It should be noted that comments on the draft guidance will not be considered during consultation on the extension to the deferred funding period.

26. Following this consultation, the Final appraisal Determination will be open to appeal for the standard 3 week period.

National Institute for Health and Care Excellence

November 2014

Appendix A

Draft guidance of the use of sofosbuvir for chronic hepatitis C

1.1 Sofosbuvir is recommended as an option for treating chronic hepatitis C in adults, as specified in table 1.

Table 1 Sofosbuvir for treating adults with chronic hepatitis C

	Sofosbuvir in combination with peginterferon alfa and ribavirin		**Sofosbuvir in combination with ribavirin**	
Genotype	**Treatment history**	**Recommendation**	**Treatment history**	**Recommendation**
Adults with genotype 1 HCV	All	**Recommended**	All	Not recommended
Adults with genotype 2 HCV	All	Not licensed for this population	Treatment-naive	**Only recommended in people who are intolerant to or ineligible for interferon**
			Treatment-experienced	**Recommended**
Adults with genotype 3 HCV	Treatment-naive	**Only recommended in people with cirrhosis**	Treatment-naive	**Only recommended in people with cirrhosis who are intolerant to or ineligible for interferon**
	Treatment-experienced	**Recommended**	Treatment-experienced	**Only recommended in people with cirrhosis who are intolerant to or ineligible for interferon**
Adults with genotype 4, 5, or 6 HCV	All	**Only recommended in people with cirrhosis**	All	Not recommended

HCV: hepatitis C virus

Treatment-naïve: the person has not had treatment for chronic hepatitis C

Treatment-experienced: the person's hepatitis C has not adequately responded to interferon-based treatment

Appendix B

Application from NHS England for an extension to the deferred funding period for sofosbuvir for chronic hepatitis C

NHSE England letter of 19 November 2014

Dear <<personal information removed>>

Waiver for NICE TA for Treatment for Hepatitis C Technology Appraisals

Thank you for your email 18 November 2014 requesting clarification on the length of the extension requested on the proposed waiver of the 90 day implementation post publication of the NICE TA for Sofosbuvir (ID654). I am replying on behalf of James Palmer, Clinical Director Specialised Services. The request as you know relates to the ability of the NHS to effectively implement this TA across England within a 90 day timeframe. As requested we have listed below the actions and progress made on the mitigations that are being implemented should a waiver be agreed.

The activities identified within the waiver application are being taken forward and an update is provided below.

1. NHS Capacity to deliver implementation of the guidance

1.1 Commissioning across organisations: Commissioners involved in the diagnostic and treatment hepatitis C pathway include NHS England Specialised, Health & Justice, Public Health England, Local Authorities and Clinical Commissioning Groups and Primary Care. NHS England has set up a Hepatitis C Task & Finish Group to bring together those involved in commissioning services involved in the Hepatitis C pathway to clarify responsibilities and to agree a coherent set of priorities. The group will also test some of the assumptions on the long term cost effectiveness of treatment and the impact this has on current costs in the acute sector of treating Hepatitis related liver failure. NICE is invited to be a member of this group.

Progress: This group is established and the Chair is Celia Ingham Clark, Clinical Director for reducing premature mortality. The first meeting is 20.11.14 and three further dates have been confirmed. This is a short life group that will report by March 2015. Actions arising from the Group will be implemented during 2015/16.

High quality care for all, now and for future generations

1.2 A Hepatitis C Network Model: NHS England working with the Hepatitis C experts drawn from its national Clinical Reference Groups has proposed the commissioning of Hepatitis C Networks in England. A Hepatitis C network model will be formally commissioned comprising specialised centres with a caseload to develop and maintain expertise in the treatment of the condition working in partnership with a range of providers across the health and justice system. This will optimise partnership working and utilisation of local expertise in engaging hard to reach groups in completing treatment programmes. A key part of the model is partnership working and the preferred procurement model would be to allow bidders additional time to develop their proposals jointly with others e.g. prison health, LAs etc.

Progress: The Hepatitis C Network proposal requires additional funding through contracts so the funding implications are being taken through NHS England's

internal approval processes. There are a number of stages and this proposal is part way through the authorisation process and will be considered for final prioritisation at the December 2014 meeting of the Clinical Prioritisation Advisory Group. The recommendations from this group will be considered by NHS England Board in January 2015. We have been advised that NHS England would be required to commission Hepatitis C Networks through a competitive procurement route. Initial advice from our procurement team envisaged this could take about 12 months but this has been revised to 9 months from November 2014.

1.3 A National database and Dashboard: To ensure Evidence Based care each Network would be required to support development of a national database of treatment and collection of outcomes to inform future treatment and commissioning of clinically effective care. A national Dashboard is already being developed for 2015/16 that will provide evidence of the reduction in harm from increased treatment of hepatitis C.
Progress: External support has been commissioned to support completion of all draft dashboards has been awarded and the dashboard will then go live within the next 3 months.

1.4 Provider Capacity: The historic low uptake of both testing and treatment means that providers have stated they would need to increase staff resources particularly specialist pharmacy and nurse specialist support in order to treat the expected increase in demand. The network proposal includes costing to support the need to increase core staff within Networks.
Progress: The financial implications are being considered as described in 1.2 and provider implementation plans will be included as part of the tender procedures *High quality care for all, now and for future generations*

In summary the timeline of an end date of August 2015 fits with our timescales to support implementation.

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NHSE England letter of 4 November 2014

Dear <<Personal information removed>>

Waiver for implementation of NICE TA for Treatment for Hepatitis C

Thank you for meeting with us to discuss the request for a 90 day waiver NHS England has made through the Department of Health.

As we discussed NHS England has requested a waiver on the 90 day implementation post publication of the NICE TA for Sofosbuvir (ID654) and this relates to the ability of the NHS to effectively implement this TA across England within a 90 day timeframe. As requested we have listed below the mitigations that would be implemented should a waiver be agreed.

Mitigations to address the issues identified within the waiver application.
If a waiver was granted the following activities would be undertaken during the agreed period.

1. **NHS Capacity to deliver implementation of the guidance**

   Commissioning across organisations. The commissioning of care for patients across the pathway includes many components of care delivery in different health settings. Commissioners involved in the diagnostic and treatment hepatitis C pathway include NHS England Specialised, Health & Justice, Public Health England, Local Authorities and Clinical Commissioning Groups and Primary Care. It is estimated that 70% of outpatient attendance costs are met outside of NHS England, however the cost of all hepatitis C drug treatments are met by NHS England. In order to address the range of commissioning arrangements to ensure a consistent approach and joined up service models that benefit patients NHS England has set up a Hepatitis C Task & Finish Group to bring together those involved in commissioning services involved in the Hepatitis C pathway to clarify responsibilities and to agree a coherent set of priorities. The group will also test some of the assumptions on the long term cost effectiveness of treatment and the impact this has on current costs in the acute sector of treating Hepatitis related liver failure. NICE is invited to be a member of this group. This group would operate between November 2014 and March 2015 but actions arising from the meeting will be implemented during 2015/16.

   A Hepatitis C network model. NHS England working with the Hepatitis C experts drawn from its national Clinical Reference Groups has proposed the commissioning of Hepatitis C Networks in England. The current provision of treatment services for patients with Hepatitis C often occurs as an adjunct to the delivery of other services including HIV, drug and alcohol, sexual health and prison health services, as well as within gastroenterology and specialist hepatology services. A Hepatitis C network model will be formally commissioned comprising specialised centres with a caseload to develop and maintain expertise in the treatment of the condition working in partnership with a range of providers across the health and justice system. The Centres will encompass MDT decision-making by experienced teams on the appropriateness of initiation of

treatment or continued surveillance of infected patients. MDT decision-making by experienced teams will support selection of the optimal treatment regimen for each patient. MDTs offer clinical and cost effective prescribing of high cost drug treatments in accordance with NHS England policy / NICE TAs. The network will support access to treatment services locally through formal partnership and outreach models. This will optimise partnership working and utilisation of local expertise in engaging hard to reach groups in completing treatment programmes. NHS England would be required to commission Hepatitis C Networks through a competitive procurement route. This process would take about 9 months. A key part of the model is partnership working and the preferred procurement model would be to allow bidders additional time to develop their proposals jointly with others e.g. prison health, LAs etc.

A national database and dashboard. To ensure evidence based care each Network would be required to support development of a national database of treatment and collection of outcomes to inform future treatment and commissioning of clinically effective care. Currently drug treatment may be offered by a variety of providers across the healthcare system, with very different levels of hepatology experience. The usually slow development of liver diseases has meant that there can be good clinical reasons for deferring treatment rather than offering the current treatments, however these decisions are dependent on robust surveillance and recall systems which are not yet in place. Patients include significant cohorts who have co-morbidities or have failed treatments previously and these patient groups require specialist input. Nationally centres will support development of a treatment stratification approach. A national Dashboard is already being developed for 2015/16 that will provide evidence of the reduction in harm from increased treatment of hepatitis C.

Provider capacity. The historic low uptake of both testing and treatment means that providers have stated they would need to increase staff resources particularly specialist pharmacy and nurse specialist support in order to treat the expected increase in demand. The network proposal includes costing to support the need to increase core staff within Networks.

2. Prevalent Demand

The management and treatment of Hepatitis C is an NHS England priority. The most recent national estimates suggest that around 160,000 adults are chronically infected with hepatitis C (HCV) in England in 2012. Current numbers of patients treated are estimated at 5,000 per year in England – 3% of those currently infected but this will increase rapidly. The CRG Hepatitis C sub group have estimated that 10 - 15,000 people per year may come forward seeking HCV treatment. As already described any clinician can prescribe under NICE TA guidance, hence given the wide range of clinicians seeing patients who also have hepatitis C it is difficult to estimate the expected pattern of prescribing across the new products coming to market.

The drivers for significant demand are:

- A pipeline of effective, low side effect, combination drug therapies which will start to be available for use from 2015 and the assumption NICE is likely to give positive Technology Appraisals on a range of new high cost products which NHS England will be required to fund if no waiver is granted.
- The demand for treatment will increase rapidly due to the high number of patients diagnosed but electively not treated in the past.
- Low control of prescribing decisions which are made across a wide range of health care and other settings mean patients may not be offered the most clinically effective treatment options.
- NHS policy initiatives already in place, or being proposed, to screen high risk groups and to raise public awareness in order to reduce the pool of people with HCV in the population and who could pass on infection.

Until last year, treatment for HCV has depended on a combination of two relatively low cost drugs – interferon and ribavirin. These have limited efficacy for some large subgroups of patients with Hepatitis C, and for many patients, cause serious side effects. There are other patients who have failed first line treatment who would now be potentially treatable with the new drugs. Patient groups are very aware that new and less toxic drugs will be available soon and there is already reported increased demand for these treatments. Over the next twelve months several directly acting anti-viral agents will be launched into the UK which will have reduced length of treatment, and side effects and increased cure / SVR rates. These drugs have different modes of action to the current treatments and allow for an interferon free (i.e. needleless) treatment strategy.

NHS England believes that the introduction of new Hepatitis C treatments will fundamentally change how we treat those affected. However, in order to ensure that the services we provide are both fit for purpose and can deliver these new treatments that ensure best outcomes for our patients we feel it is imperative that we are given sufficient time to implement the strategy outlined above before we are required to fund drugs that may be used inappropriately and to ensure systems are in place to collect outcomes data to inform future clinical practice.

Yours sincerely,

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