NHS England

PRIVATE BOARD PAPER - NHS ENGLAND

Title: New Drugs for Hepatitis C

From: Bruce Keogh, National Medical Director

Rationale for this paper being discussed in the private session:

- Commercial confidentiality

Purpose of paper:

- The Paper is to inform the Board of the future cost implications of new Hepatitis C treatments including Sofosbuvir, and provide options for mitigation.

Actions required by the Board:

- Note the cost impact of new drug treatments entering the market for Hepatitis C, consider the range of mitigating actions and agree the proposed strategy based on the recommendations.

New Drugs for Hepatitis C

Executive summary

1. Several new treatments for Hepatitis C will be launched into the UK market over the next 12 months. It is anticipated that all these new therapies will be supported by NICE Technology Appraisals and as such there will be a statutory requirement to fund the drugs.

2. NICE is due to publish its recommendations on the first of these new drugs, Sofosbuvir, in November. NHS England has responded as part of the consultation to the draft guidance.

3. The average treatment cost for a patient will rise from [redacted] for current treatments to [redacted] depending on the treatment chosen, which itself will depend on the patient's Hepatitis C status.

4. The Specialised Services Clinical Reference Groups has advised that the number of patients who will request treatment will rise significantly over the next 12-18 months. This, coupled with the increased drug price, suggests that the cost of treating Hepatitis C will rise from circa [redacted] per annum to over [redacted] by the end of 2016/2017

5. The Board is asked to support a proposed strategy; this will involve a number of components with the aim of mitigating the potential costs to the NHS over the next 4-5 years. The key areas of work, all of which would need to be actioned, are as follows:

    - Continue to support urgent cases only, working with NICE and DH to secure a waiver to the 90 day rule for implementation of NICE Technology Appraisals to at least a year.
    - Limit access to specialised centres and stratify treatments to ensure the most cost effective product is selected for every patient.
    - Reduce the cost burden through a medicine procurement tender to secure best value prices and utilise the PPRS agreement to maximal benefit.

Actions required by the Board:

- Note the cost impact of new drug treatments entering the market for Hepatitis C, consider the range of mitigating actions and agree the proposed strategy based on the recommendations.

Background

Epidemiology

1. There are approximately 160,000 people chronically infected with hepatitis C virus (HCV) in England. Fewer than half of them have been diagnosed and others have electively declined current treatments. The majority of the hepatitis C population is made up of IV drug users and migrants. Hepatitis C infection usually causes slowly progressive liver disease, leading over 20 - 30 years to severe liver damage and liver failure in some patients. The infected population covers a spectrum from mild disease, which will take many years to cause harm, to terminal liver disease. Patients with advanced disease require high cost inpatient care, which may include liver transplantation (140 HCV patients are on the liver transplant list): the proportion with severe disease is increasing as the rate of new infections has significantly increased as a result of the growth in IV drug use from the 1970s.

Drivers of demand

2. The demand for treatment of patients with Hepatitis C will present a significant issue of affordability to the NHS due to 5 inter-related factors.

    - A pipeline of effective, low side effect, combination drug therapies which will start to be available for use from 2015.
    - NICE giving positive Technology Appraisals on these high cost products which NHS England will be required to fund.
    - 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.
    - NHS policy initiatives already in place, or being proposed, to reduce the pool of people with HCV in the population and who could pass on infection.

3. Current numbers 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[1].

4. Unmet demand: Until recently, treatment for HCV has depended on a combination of two 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 potentially be 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. The estimate of 10,000-15,000 coming forward represents less than 10% of the estimated infected population.

[1] This estimate is based on the number of patients diagnosed, but not currently treated due to toxicity or other contra-indications.

5. Prescribing: The treatment of Hepatitis C often occurs under the umbrella of other services treating infectious diseases, sexual health and substance misuse, as well as in liver services. Decisions on treatment can be made in all these settings in line with NICE guidance, with the drug costs falling to specialised commissioning. The NICE guidance for the new drug therapies will potentially allow treatment without the involvement of clinicians who specialise in the treatment of Hepatitis C.

6. Public Health England has identified the reduction of Hepatitis C in the population as a high priority, in order to reduce the high cost of inpatient treatment for liver disease in the long term and to reduce onward transmission of the virus in the population. Successfully treated patients cease to pose a risk of infection to others, including health workers. The availability of these new and effective treatments means this aim is now a feasible goal, subject to funding. NHS Health & Justice, sexual health and substance misuse services are increasing active case-finding, including initiatives such as 'opt out' testing for prisoners in England being introduced in 2014. Initially this will have a small effect on the numbers diagnosed but is already increasing case identification which will translate into demand for treatment.

Current treatment options and costs

7. The accepted goal of therapy is to achieve a "sustained virological response" (SVR) as a proxy for a cure. Confirmation that an SVR has been achieved at week 12 following completion of treatment (SVR12) is now accepted by most clinical and regulatory authorities as the primary indication that the patient has cleared their virus.

8. Currently, two main treatment regimens provide the standard of care for patients with chronic Hepatitis C (CHC) infection in the UK. These are Interferon based combinations of dual or triple therapy, requiring injections over 24 or 48 weeks. The choice of treatment is dependent on clinical factors.

9. For current therapies SVR / cure rates range from 80% to as low as 40% depending on subtype, disease progression and co-infections.

10. It is difficult to provide a completely accurate figure for the current spend on CHC treatments. An estimate based on current numbers treated and average cost of drugs is that NHS England spends between £65 to £75m.

Future treatment options and costs

11. 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.

Table 1 provides information on the status of each drug including anticipated NICE publication.

Drug	Company	License status	NICE publication Date	[redacted]
Sofosbuvir	Gilead	Licensed	Nov 2014	[redacted]
Simeprevir	Janssen	Licensed	January 2014	[redacted]
Daclatasvir	BMS	Licensed	August 2015	[redacted]
Sofosbuvir + Ledipasvir	Gilead	3rd qtr 14/15	June 2015	[redacted]
ABT-450/Ritonavir Ombitasvir/Dasabuvir	Abbvie	4th qtr 14/15	June 2015	[redacted]

12. All the above products are being considered by NICE under its Technology Assessment process. Sofosbuvir as a combination therapy has already been considered by NICE and a second Appraisal Consultation Document (ACD) has recommended it as an option for the treatment of CHC across a range of subtypes. At a cost of [redacted] for a Sofosbuvir combination therapy, the predicted spend at current treated numbers has been estimated at [redacted] If numbers, as expected, increase to 10-15,000 patients treated per annum then the anticipated costs rise to [redacted] at current prices. If drugs are combined at an average price of [redacted] the estimated cost of treating 10-15,000 patients per year could rise to [redacted] These estimates are based on less than 10% of the infected population being treated. If diagnosis rates increase above this rate, then these costs may be a significant under-estimate.

Table 2 Projected Drug costs (ex VAT)

Patients Per year	Current Cost per patient £ 15k	Cost per patient £ 38k	Cost per patient £50k	Cost per patient £55k
	[redacted]	[redacted]	[redacted]	[redacted]
5,000	[redacted]	[redacted]	[redacted]	[redacted]
10,000		[redacted]	[redacted]	[redacted]
15,000		[redacted]	[redacted]	[redacted]

14. NHS England has responded to the draft NICE guidance for Sofosbuvir. (The response is attached as appendix 1).

The NICE process

15. NICE can review medicines as either single or Multiple Technology Appraisal (MTA) processes, where there are multiple technologies for the same condition, as in the case of Hepatitis C. NHS England would expect NICE to undertake an MTA in 2016, if not before, on the Hepatitis C products to be launched over the next 12 months.

Strategy for managing the cost impact of new Hepatitis C treatments

16. There are a number of actions which need to be progressed over a range of timescales. These are grouped under themes set out below. It is important to note that the proposed strategy is to take forward all these actions in order to manage the budgetary impact facing NHS England over the next 4-5 years. Each area has specific issues that are likely to be raised and will require resolution.

Secure a waiver to the 90 day implementation period and focus on the treatment of high risk patients.

17. It is an obligation for NHS England, as the direct commissioner of Hepatitis C treatments, to fund NICE TA decisions within 90 days.

18. NHS England has requested a waiver to 90 day implementation through its response to the Sofosbuvir ACD (appendix 1). NICE will need to consider this request and consult with the SoS to extend the implementation date.

19. A request for an extension of a minimum of 12 months should be made, to enable services to be reconfigured. It is understood that DH are sympathetic to this request given the significant cost of implementation.

20. A cross organisational "Hep C Taskforce" has been set up to ensure there is shared understanding of the affordability issues and support for an agreed way forward, to balance the desire for access to the new and better treatments within the available resource.

21. During this period the current NHS England policy for delivering treatment to patients with liver failure, close to needing a liver transplant, would continue.

22. This initiative delivers the lowest financial risk to NHS England in the short term while formal specialised centres and networks are established (see below). NHS England will continue to treat those patients who are at significant risk, estimated to be circa 10 per month, within current budget.

Implement formal arrangements for specialised centres and networks.

23. To ensure that the most appropriate and cost effective treatments are selected, the prescribing of new drugs should be limited to specialised centres working collaboratively as part of Hepatitis C networks. Centres will have access to Hepatitis C MDTs and specialist nurse input to oversee treatment options and drug regimen selection. This model is partially in place in some areas so would need to be formally commissioned to achieve national adoption, and could be procured during 2015.

24. As the patient cohort expands, services also need to be expanded and developed ; this cannot be appropriately and safely achieved in the 90 day NICE TA timeframe, hence the requirement for managed market entry.

25. NHS England, in its response to the Sofosbuvir ACD (appendix 1) have requested that NICE includes a statement within the final guidance that limits access to the new

Hepatitis C drugs to specialist centres. This is supported by the Hepatitis C CRG sub group.

26. The Hepatitis C CRG sub-group should produce recommendations for when and which treatments should be offered to patients and at which point in the pathway. Hepatitis C networks will adopt this guidance on stratification of treatments to allow the most cost-effective treatment to be selected. This will include a "watch and wait" programme for patients who do not require immediately clearance of their virus to prevent ongoing harm on clinical grounds.

27. The stratification of treatments will require complete clinician and patient group support as most, if not all of these drugs will be NICE approved and therefore available for clinicians to prescribe. The Hepatitis C taskforce group will support engagement of the key stakeholders working with the specialised Clinical Reference Groups.

28. The stratification algorithm should be in place by September 2015 to include all drugs that will be launched over the next 12 months.

29. It is estimated that a stratification strategy, coupled with controlled entry, will reduce the impact of the new medicines by circa [redacted] per annum depending on the level of growth (Table 3)

Controlling the costs of the new Hepatitis C medicines

30. NHS England will work with the DH Commercial Medicines Unit to tender the drugs coming to market with the aim of securing lower prices. In order to cover all the drugs coming to market over the next 12 months tendering will need to commence mid-2015.

31. This will mean new prices, if offered, would be available from January 2016. It is difficult to estimate the impact of the tender but similar tenders for HIV products have released circa [redacted] savings over the last 5 years.

32. In addition to the mitigations set out above, the use of the Pharmaceutical Price Regulation Scheme (PPRS) could be used to further mitigate costs. This is a five year scheme to eliminate the effect of growth in the use of branded drugs on NHS budgets.

33. The scheme involves Pharma paying HM Treasury (HMT) the value of any increase in the use of branded drugs. HMT provides a supplement to NHS England to reflect the projected receipts from Pharma under this scheme. In the case of increased branded drug use, over and above current assumptions, Pharma have to increase the payment made to HMT. However, the current mechanism does not allow for these additional HMT receipts to be made available to NHSE as a pass through payment.

34. If such a pass through arrangement could be negotiated, this would eliminate the additional costs to NHS England of the Hepatitis C drugs that are covered by PPRS. [redacted]

[redacted]

Summary and Recommendations

35. Mitigation of the cost impact of new drug treatments for Hepatitis C will require a range of actions over the short and medium term. The potential for mitigation is summarised below.

Table 3

36. The Board is asked to support the proposed strategy. This will involve:

- Working with NICE and DH to secure the waiver to the 90 day rule to at least a year.
- Supporting the proposal to establish formally identified specialist centres and networks and introduce stratified treatment regimes
- Procurement of Hepatitis drugs to secure best value prices.
- Working with DH to utilise the PPRS agreement to its maximal benefit

Appendix 1

NHS England Response to NICE ACD – Sofosbuvir for treating chronic hepatitis C (ID654)

NHS England would like to provide the following response to the ACD – Sofosbuvir for treating chronic hepatitis C.

NHS England is generally supportive of the recommendations contained within the ACD. Whilst we recognise some of the limitations of the RCTs performed in some genotypes we also recognise that Sofosbuvir within the recommendations falls well within the accepted QALY threshold. We would like to raise the following points for consideration by NICE:

1. The wording in a number of the conclusions is that 'Sofosbuvir is recommended *as an option* for…' but it is essential that treatment decisions are made by clinicians experienced in the management of hepatitis C (preferably working as a team through MDT meetings), to ensure that the most appropriate and cost effective treatments are used.

NHS England would expect that this is included in the recommendations.

2. The criteria relating to Sofosbuvir with Ribivirin needs to be more explicit. Given the cost of such treatment could be circa £70k per patient course we are concerned that the definition of *'Interferon unsuitable – includes people who are intolerant to and ineligible for Interferon'* could lead to wide interpretation and would lead to overuse of this combination. This regimen should clearly be seen as a second line therapy, for patients who are truly unable to take interferon.

NHS England would expect the criteria to be changed to exclude naïve patients unless they have a specific contraindication to pegylated Interferon and that there is further refinement of the definition of 'interferon unsuitable'.

3. We note that Genotype 2 is not mentioned at all in the summary of treatment recommendations for Sofosbuvir/pegylated Interferon/Ribivirin. Whilst we appreciate that evidence is limited in this group, for completeness there should be some statement as to whether or not NICE recommends this treatment as an option in Genotype 2.

NHS England asks that a statement as to the suitability of Sofosbuvir for Genotype 2 is included in the recommendations.

4. NHS England would like to seek a waiver to the period within which NICE TAs are funded (i.e. within 3 months). The first reason for the request for an extension relates partly to the capacity of the NHS to meet what is expected to be an increased demand for drugs such as Sofosbuvir. In other words, NHS England believes that the health technology cannot be appropriately

administered until other appropriate health services resources, including staff, are in place. This includes the ability to monitor the results of treatment i.e. recording and reporting of a sustained virological response rate. The second reason is because at the prices proposed by the manufacturer in their NICE submission, this technology is not affordable at the quantum of new expenditure it would represent (particularly if the backlog of prevalent cases become immediately eligible for funding alongside incidence cases). The third reason is because further therapies for Hepatitis C are likely to become available in the foreseeable future, and the NHS would wish to see their comparative cost effectiveness assessed before selecting one particular option for hundreds of millions of pounds of new public investment.

NHS England formally requests a waiver or substantial extension over several years to the normal implementation period for the reasons given above.