NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA75; Interferon alfa and ribavirin for treating chronic hepatitis C, TA106; Peginterferon alfa and ribavirin for treating mild hepatitis C, and TA200; Pegylated interferons, peginterferon alfa, ribavirin and alfa interferon for treating hepatitis C

This guidance was issued in: TA75 (January 2004); TA106 (August, 2006); TA200 (September, 2010)

The review date for this guidance is: TA75 and TA106 (no date given); TA200 (July, 2013)

1. Recommendation

The guidance should be transferred to the 'static guidance list' until the start of the development of the clinical guideline. That we consult on this proposal.

2. Original remit(s)

TA75: The use of this technology for mild CHC (and any consequent changes that this may have on this guidance) will be considered after the publication of the results of the two relevant clinical trials, and at the earliest in August 2004. The full guidance will be reviewed in November 2006.

TA106: The use of this technology for mild CHC (and any consequent changes that this may have on this guidance) will be considered after the publication of the results of the two relevant clinical trials, and at the earliest in August 2004. The full guidance will be reviewed in November 2006.

TA200: To review, and update as necessary, the Institute's current guidance on the clinical and cost-effectiveness of peginterferon alfa and ribavirin for the treatment of chronic hepatitis C.

3. Current guidance

TA75

1.1 Combination therapy with peginterferon alfa and ribavirin is recommended within its licensed indications for the treatment of people aged 18 years and over with moderate to severe chronic hepatitis C (CHC), defined as histological evidence of significant scarring (fibrosis) and/or significant necrotic inflammation.

1.2 People with moderate to severe CHC are suitable for treatment if they have:

- not previously been treated with interferon alfa or peginterferon alfa, or

- been treated previously with interferon alfa (as monotherapy or in combination therapy), and/or

- ~~previously received peginterferon alfa monotherapy only and responded at the end of treatment but subsequently relapsed, or did not respond at the end of treatment.~~ (This part recommendation has been updated and replaced by NICE technology appraisal guidance 200)

1.3 People currently being treated with interferon alfa, either as combination therapy or monotherapy, may be switched to the corresponding therapy with peginterferon alfa.

1.4 Treatment for the groups identified in Sections 1.1 and 1.2 should be as follows.

- People infected with hepatitis C virus (HCV) of genotype 2 and/or 3 should be treated for 24 weeks.

- For people infected with HCV of genotype 1, 4, 5 or 6,initial treatment should be for 12 weeks. Only people showing, at 12 weeks, a reduction in viral load to less than 1% of its level at the start of treatment (at least a 2-log reduction, see Section 4.1.2.5) should continue treatment until 48 weeks. For people in whom viral load at 12 weeks exceeds 1% of its level at the start of treatment, treatment should be discontinued.

- People infected with more than one genotype that includes one or more of genotypes 1, 4, 5, or 6 should be treated as for genotype 1.

(Recommendation 1.4 still applies for people who are treated with standard courses of combination therapy, but has been replaced by NICE technology appraisal guidance 200 (TA200) for people who are eligible for shortened courses of combination therapy (as described in recommendation 1.2 of TA200)

1.5 People satisfying the conditions in Sections 1.1 and 1.2 but for whom ribavirin is contraindicated or is not tolerated should be treated with peginterferon alfa monotherapy. Regardless of genotype, individuals should be tested for viral load at 12 weeks, and if the viral load has reduced to less than 1% of its level at the start of treatment, treatment should be continued for a total of 48 weeks. If viral load has not fallen to this extent, treatment should stop at 12 weeks.

1.6 People for whom liver biopsy poses a substantial risk (such as those with haemophilia, or those who have experienced an adverse event after undergoing a previous liver biopsy), and people with symptoms of extra-hepatic HCV infection sufficient to impair quality of life, may be treated on clinical grounds without prior histological classification.

1.7 There is insufficient evidence to recommend combination therapy using peginterferon alfa or interferon alfa in people who:

• ~~have previously been treated with combination therapy using peginterferon alfa, and/or~~ (This part recommendation has been updated and replaced by NICE technology appraisal guidance 200)

• are younger than 18 years of age, and/or

• have had a liver transplantation. Treatment of CHC recurrence after liver transplantation (whether or not the person had been treated with interferon alfa or peginterferon alfa therapy at any time before transplantation) should be considered as experimental and carried out only in the context of a clinical trial.

TA 106

1.1 Combination therapy, comprising peginterferon alfa-2a and ribavirin or peginterferon alfa-2b and ribavirin, is recommended, within the licensed indications of these drugs, for the treatment of mild chronic hepatitis C.

1.2 Monotherapy with peginterferon alfa-2a or peginterferon alfa-2b is recommended, within the licensed indications of these drugs, for the treatment of mild chronic hepatitis C for people who are unable to tolerate ribavirin, or for whom ribavirin is contraindicated.

1.3 The decision on whether a person with mild chronic hepatitis C should be treated immediately or should wait until the disease has reached a moderate stage ('watchful waiting') should be made by the person after fully informed consultation with the responsible clinician. The decision to treat need not depend on a liver biopsy to determine the stage of the disease if treatment is initiated immediately. However, a biopsy may be recommended by the clinician for other reasons or if a strategy of watchful waiting is chosen.

~~1.4 The duration of treatment should vary according to the licensed indications of the chosen drug, the genotype of the virus, the initial viral load, the response to treatment, and the treatment regimen chosen.~~

~~1.5 Second or subsequent courses of treatment are not recommended for people who have been treated with a first course of either combination therapy or monotherapy with peginterferon alfa if they have not had an early response (as indicated by reduction in viral load at 12 weeks).~~

(Recommendations 1.4 and 1.5 have been updated and replaced by NICE technology appraisal guidance 200)

1.6 There is insufficient evidence to recommend combination therapy or monotherapy with peginterferon alfa for people with mild chronic hepatitis C who are under the age of 18 years, or those who have had a liver transplant.

TA 200

1.1 Combination therapy with peginterferon alfa (2a or 2b) and ribavirin is recommended as a treatment option for adults with chronic hepatitis C:

- who have been treated previously with peginterferon alfa (2a or 2b) and ribavirin in combination, or with peginterferon alfa monotherapy, and whose condition either did not respond to treatment or responded initially to treatment but subsequently relapsed or
- who are co-infected with HIV.

1.2 Shortened courses of combination therapy with peginterferon alfa (2a or 2b) and ribavirin are recommended for the treatment of adults with chronic hepatitis C who:

- have a rapid virological response to treatment at week 4 that is identified by a highly sensitive test and
- are considered suitable for a shortened course of treatment.

1.3 When deciding on the duration of combination therapy, clinicians should take into account the licensed indication of the chosen drug (peginterferon alfa-2a or peginterferon alfa-2b), the genotype of the hepatitis C virus, the viral load at the start of treatment and the response to treatment (as indicated by the viral load).

4. Rationale[1]

No new evidence has been identified that is likely to fundamentally change the recommendations in TAs 75, 106 and 200. However, the recommendations for the use of peginterferons and ribavirin are now very fragmented (with elements being updated in subsequent guidance) and will be even more so once the ongoing technology appraisal of the use of the drugs in children has been published, which will update recommendation 1.6 in TA106. It would therefore be beneficial to bring the current TA recommendations together as part of the wider clinical context, and that is best done through a guideline.

The new evidence is related to 4 small studies comparing the effectiveness of peginterferon alfa-2a with peginterferon alfa-2b, and studies investigating the role of polymorphisms in the interleukin 28 gene. Consideration of both these issues would be better accommodated in the context of the ongoing clinical. It is therefore proposed that the current recommendations of TAs5, 106 and 200 are transferred to

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

the ‘static guidance list’ until the start of the development of the clinical guideline for the management of hepatitis C.

5. Implications for other guidance producing programmes

A guideline on Hepatitis C has recently been referred to NICE (http://guidance.nice.org.uk/CG/Wave0/666) and is currently in the scoping phase. At a recent workshop, stakeholders indicated that the guideline should not be produced at this time until after a number of new technologies have been assessed by the technology appraisal programme (e.g. sofosbuvir). This is because these new technologies have the potential to transform the management of the disease in the future. CCP are consulting with stakeholders on whether we should delay producing this guideline until newer interventions can be assessed as part of the Technology Appraisal Programme.

6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from June, 2009 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the ‘Summary of evidence and implications for review’ section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

The marketing authorisation for peginterferon-2a (Roche) was extended in March 2013 to include paediatric patients aged 5 years and over. The marketing authorisation for peginterferon-2b (Merck, Sharp and Dohme) was extended to include paediatric patients aged 3 years and older and adolescents in November 2009. These licence extensions are being considered in a separate currently ongoing appraisal. The marketing authorisation for peg-interferon-2b was also recently extended to include ‘tri-therapy’ in adults, that is, in combination with ribavirin and boceprevir, for treating chronic hepatitis C genotype-1 in adults with compensated liver disease. This latter amendment to the marketing authorisation was considered in a separate technology appraisal (NICE Technology Appraisal No. 253). Therefore there have been no changes to marketing authorisations that directly affect the current recommendations in TA75, 106 and 200.

A large number of studies were identified in a literature search that included published journal articles from 2009 onwards (more than 550 journal articles identified). Many of the studies were not directly relevant because they cover the use of the drugs outside the remit of TAs 75,106 and 200. Some studies were identified that looked at durations of treatment in specific subgroups but the studies largely supported the existing recommendations in the current guidance. A number of studies were identified that compared the effectiveness of peginterferon alfa-2a with peginterferon alfa-2b (Ascione et al 2010; Kamal et al 2011; Mach et al 2011; Miyase et al 2012). These studies included between 200 and 320 patients and some of the studies suggested that there could be differences in efficacy between the two different peginterferons. Several meta-analyses have also been published in this area indicated a possible improved virological response for peginterferon alfa-2a

compared with peginterferon alfa-2b. Consideration of the comparative efficacy of peginterferon alfa-2a and 2b would more appropriate in the context of a clinical guideline.

Several studies were identified the role of polymorphisms in the interleukin 28 gene in predicting clearance of hepatitis C or treatment response indicating that testing for these polymorphism might help tailoring treatments depending on the hepatitis genotype. However, consideration of this would be better accommodated in the context of a clinical guideline.

8. Implementation

A submission from Implementation is included in Appendix 3.

Since publication of the original technology appraisal (TA 75) there has been an increase in the cost and volume of peginterferon, which has subsequently tailed off following the publication of TA200. Coinciding with this trend the cost and volume of non-pegylated interferon has declined. Use of ribavirin remained fairly constant since publication of the original guidance. This information indicates that NICE guidance is being adhered to although it is difficult to interpret the level of variation in practice from this data

9. Equality issues

No equalities issues were identified.

GE paper sign off: Elisabeth George, 24 09 13

Contributors to this paper:

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CPP/CPHE input	Ben Doak

Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed
- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Technology appraisals TA252 Telaprevir for the treatment of genotype 1 chronic hepatitis C. Issued: April 2012. Expected review date: April 2015

Technology appraisals TA253 Boceprevir for the treatment of genotype 1 chronic hepatitis C. Issued: April 2012. Expected review date: April 2015

Public health guidance PH43 Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection. Issued: December 2012. Expected review date: April 2015

In progress

Clinical guideline. Hepatitis C. Publication date still to be confirmed.

Technology appraisals Hepatitis C (children and young people) - peginterferon alfa and ribavirin [ID373] Expected date of issue: August 2013

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
	ViraferonPeg (Peginterferon alfa-2b) in combination with ribavirin and boceprevir (tritherapy) is indicated for the treatment of chronic hepatitis C (CHC) genotype 1 infection in adult patients (18 years of age and older) with compensated liver disease who are previously untreated or who have failed previous therapy. (April 2012)
	Pegasys (peginterferon alfa-2a) in combination with ribavirin is indicated for the treatment of chronic hepatitis C in treatment-naïve children and adolescents 5 years of age and older who are positive for serum HCV-RNA. When deciding to initiate treatment in childhood, it is important to consider growth inhibition induced by combination therapy. The reversibility of growth inhibition is uncertain. The decision to treat should be made on a case by case.(March 2013)

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date,)
Eltrombopag (Revolade)	For thrombocytopenia associated with hepatitis C virus
Silibinin (Legalon)	For the prevention of recurrent hepatitis C infection in liver transplant recipients
BI 201335 / Faldaprevir in combination with peginterferon alfa-2a and ribavirin	For the treatment of genotype 1 chronic hepatitis C
Simeprevir in combination with ribavirin and peginterferon alfa	For the first line treatment of genotype 1 hepatitis C
Simeprevir in combination with ribavirin and peginterferon alfa-2a	For the second line treatment of genotype 1 hepatitis C
GS-7977 / sofosbuvir	For the treatment of chronic hepatitis C infection
Faldaprevir (BI 201335) in combination with BI 207127	For the treatment of genotype 1 chronic hepatitis C
ABT-450/r/ABT-267 in combination with ABT-333	For chronic genotype-1 hepatitis C infection for patient group
Sofosbuvir/Lidepasvir	For chronic infection with genotype 1 hepatitis C virus

Registered and unpublished trials

Trial name and registration number	Details
Pegylated Interferon Alfa-2a Plus Low Dose Ribavirin for Treatment-Naïve Dialysis Patients With Chronic Hepatitis C (NCT00491244)	Estimated Enrolment: 352 Estimated Study Completion Date: June 2013
Randomized Controlled Open Label Trial of Peg Alpha 2a Interferon and Adjusted-dose of Ribavirin vs. Standard Therapy in the Treatment of Naive Chronic Hepatitis C Patients Infected With Genotype 4 (NCT01686789)	Estimated Enrolment: 190 Estimated Study Completion Date: June 2014

Trial name and registration number	Details
Study to Assess the Efficacy of 12 Versus 24 Weeks of Extended Treatment in HCV-Genotype 2/3 Patients (OPTEX2/3) (NCT00803309)	Estimated Enrolment: 150 Estimated Study Completion Date: March 2014
Hepatitis C in a Cohort of Patients With Maintenance Therapy for Opiate Dependence - Prevalence, Severity and Outcome of Antiviral Therapy (NCT01045278)	Estimated Enrolment: 450 Estimated Study Completion Date: May 2013
Efficacy and Safety of Short Course Therapy With Peginterferon Alpha-2b (PEG-IFN Alfa-2b) and Ribavirin (RBV) for Chronic Hepatitis C (Genotype 4) Participants Achieving a Rapid Virological Response at Week 4 of Treatment (MK-8908B-059 AM1) (START 4) (NCT01606800)	Estimated Enrolment: 160 Estimated Study Completion Date: October 2015
Peginterferon Alfa-2a and Ribavirin for Genotype 2 Chronic Hepatitis C: Duration and Ribavirin Dose Stratified by RVR (NCT00532701)	Estimated Enrolment: 962 Estimated Study Completion Date: July 2013
A Collaborative Trial in Injectors of Individualized Treatment for Genotype 2/3 (ACTIVATE) (NCT01364090)	Estimated Enrolment: 100 Estimated Study Completion Date: December 2013
Treatment of Acute Hepatitis C Virus in HIV Co-Infection (NCT00845676)	Estimated Enrolment: 20 Estimated Study Completion Date: December 2013
Response to Pegylated Interferon and Ribavirin in Chinese Patients With Chronic Hepatitis C Genotypes 1 Versus 2/3 Versus 6 (NCT01433887)	Estimated Enrolment: 500 Estimated Study Completion Date: June 2013
Safety and Efficacy Study of Peginterferon Lambda-1a vs. Peginterferon Alfa-2a, Plus Ribavirin in Subjects With Genotype 1 Hepatitis C (BASIS) (NCT01754974)	Estimated Enrolment: 300 Estimated Study Completion Date: March 2015
A Study of The Relationship Between Drop in Hemoglobin and Sustained Virological Response in Patients With Chronic Hepatitis C Treated With Copegus (Ribavirin) and Pegasys (Peginterferon Alfa-2a) (NCT01585324)	Enrolment: 30 Estimated Study Completion Date: July 2014

Trial name and registration number	Details
A Study Evaluating Slow Response/Non-Rapid Response in Patients With Chronic Hepatitis C, Genotype 1, 2, 3 & 4 Treated With Pegasys (Peginterferon Alfa-2a) and Copegus (Ribavirin) (NCT01429792)	Estimated Enrolment: 200 Estimated Study Completion Date: December 2014
Treatment of Recently Acquired Hepatitis C Virus Infection (ATAHC-II) (NCT01336010)	Estimated Enrolment: 120 Estimated Study Completion Date: April 2015
A Study of Extended Therapy of PEGASYS (Peginterferon Alfa-2a) in Combination With COPEGUS (Ribavirin) in Patients With Chronic Hepatitis C and Slow Response (NCT01033448)	Estimated Enrolment: 100 Estimated Study Completion Date: November 2015
A Study of Ribavirin in Combination With PEGASYS (Peginterferon Alfa-2a (40KD))in Patients With Chronic Hepatitis C (NCT00922779)	Enrolment: 7780 Estimated Study Completion Date: November 2013
A Randomized Trial of 24-Week Versus 48-Week Courses of Peginterferon Plus Ribavirin for Patients With Genotype 1 Hepatitis C and IL28B CC Polymorphism (NCT01441804)	Estimated Enrolment: 200 Estimated Study Completion Date: August 2013
Efficacy and Safety Study of Peginterferon Alfa-2b in Chinese Chronic Hepatitis C Patients (NCT01581398)	Enrolment: 814 Estimated Study Completion Date: April 2015
A Randomized Trial of 24-Week Versus 48-Week Courses of Peginterferon Plus Ribavirin for HCV Genotype-6 Patients (NCT01263860)	Estimated Enrolment: 260 Estimated Study Completion Date: July 2014
Algeron (Cepeginterferon Alfa-2b) Compared With PegIntron (Peginterferon Alfa-2b) for Treatment of Chronic Hepatitis C (NCT01740089)	Enrolment: 150 Estimated Study Completion Date: December 2013
Ribavirin Loading Dose or Priming and Concentration Targeting for HCV Genotype 1 (RibaC) (NCT01226771)	Estimated Enrolment: 105 Estimated Study Completion Date: June 2013
36 vs 48 Wks Peg-Intron Plus Ribavirin for HCV Patients Without Rapid Virologic Response But Without HCV RNA at wk 8 (NCT01683786)	Estimated Enrolment: 60 Estimated Study Completion Date: December 2014

References

Ascione, A., De, Luca M., Tartaglione, M. T.et al. (2010) Peginterferon alfa-2a plus ribavirin is more effective than peginterferon alfa-2b plus ribavirin for treating chronic hepatitis C virus infection. Gastroenterology 138 (1): 116-122

Awad T, Thorlund K, Hauser G *et al*. Peginterferon alpha-2a Is Associated with Higher Sustained Virological Response than Peginterferon alfa-2b in Chronic Hepatitis C: Systematic Review of Randomized Trials. *Hepatology* 2010;51:1176-1184.

Flori N, Funakoshi N, Duny Y et al. Pegylated Interferon-a2a and Ribavirin versus Pegylated Interferon-a2b and Ribavirin in Chronic Hepatitis C: A Meta-Analysis. *Drugs* 2013;73:263–277.

Kamal, S. M., Ahmed, A., Mahmoud, S.et al. (2011) Enhanced efficacy of pegylated interferon alpha-2a over pegylated interferon and ribavirin in chronic hepatitis C genotype 4A randomized trial and quality of life analysis. Liver International 31 (3): 401-411

Mach, T. H., Ciesla, A., Warunek, W.et al. (2011) Efficacy of pegylated interferon alfa-2a or alfa-2b in combination with ribavirin in the treatment of chronic hepatitis caused by hepatitis C virus genotype 1b. Polskie Archiwum Medycyny Wewnetrznej 121 (12): 434-439

Miyase, S., Haraoka, K., Ouchida, Y.et al. (2012) Randomized trial of peginterferon -2a plus ribavirin versus peginterferon -2b plus ribavirin for chronic hepatitis C in Japanese patients. Journal of Gastroenterology 47 (9): 1014-1021

Romero-Gomez M, Planas R, Ampuero J *et al*. Meta-analysis: pegylated interferon a-2a achieves higher early virological responses than a-2b in chronic hepatitis C. *AP&T* 2013 Apr 14. doi: 10.1111/apt.12314. [Epub ahead of print] - supported by a grant from Roche Farma S.A.

Rumi M, Aghemo A, Prati GM. Comparative trials of peginterferon α2a and peginterferon α2b for chronic hepatitis C. *Journal of Viral Hepatitis* 2012;19(1):37–41

Singal AK, Jampana SC, Anand BS. Peginterferon Alfa-2a Is Superior to Peginterferon Alfa-2b in the Treatment of Naïve Patients with Hepatitis C Virus Infection: Meta-Analysis of Randomized Controlled Trials. *Dig Dis Sci* 2011;56:2221–2226.

Appendix 3 – Implementation submission

Implementation feedback: review of NICE technology appraisal guidance 75, 106 & 200

NICE Technology Appraisal 75 Hepatitis C - pegylated interferons, ribavirin and alfa interferon NICE Technology Appraisal 106 Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C NICE Technology Appraisal 200 Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C
Implementation input required by 30/04/2013
Please contact Rebecca Lea regarding any queries rebecca.lea@nice.org.uk

Contents

1 Routine healthcare activity data

1.1 Hospital Pharmacy Audit Index data

This section presents data on the net ingredient cost and volume of pegylated interferon alfa, non-pegylated interferon alfa and ribavirin prescribed and dispensed in hospitals in England.

Figure 1 Cost and volume of pegylated interferon alfa prescribed and dispensed in hospitals in England

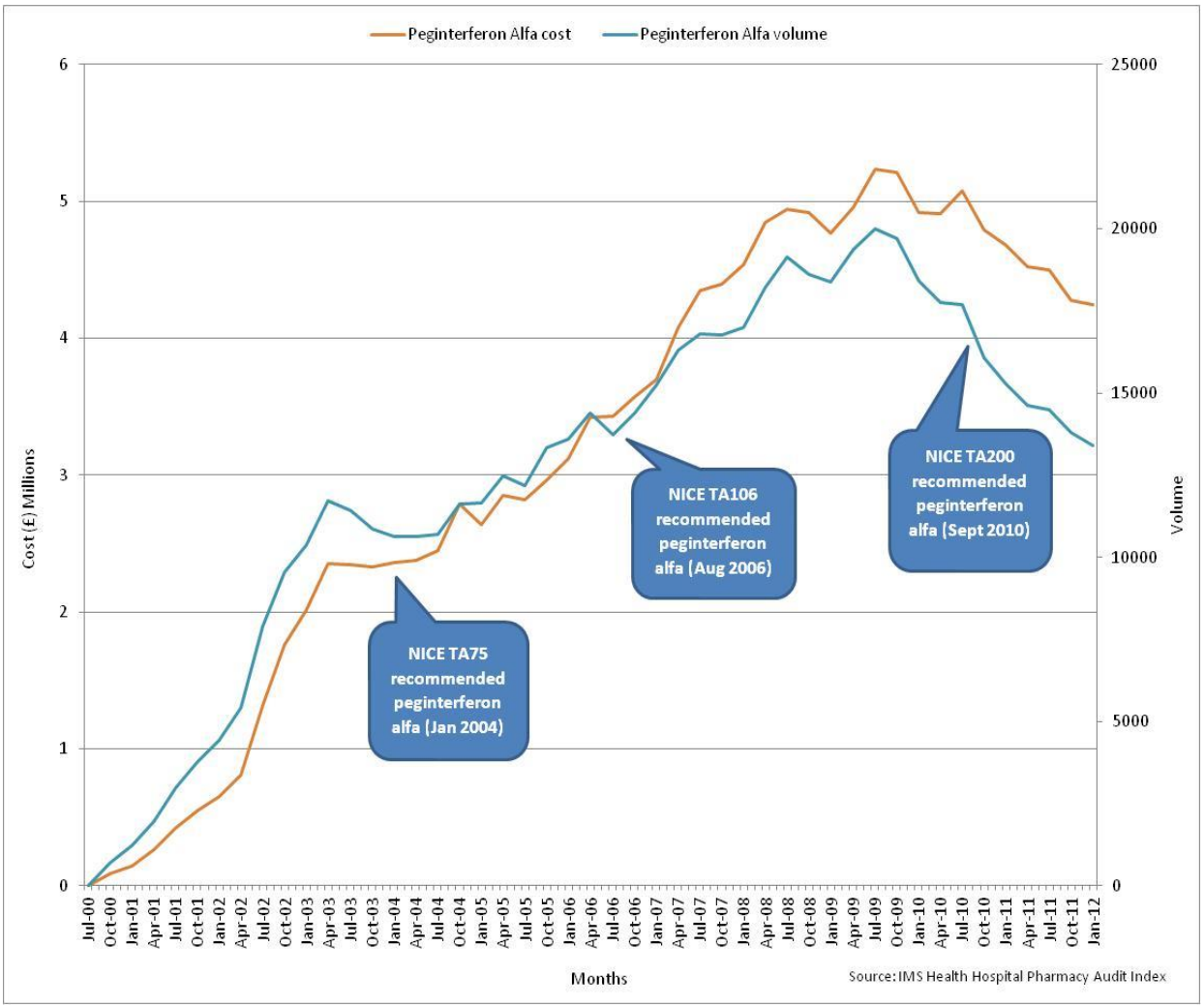


Figure 2 Cost and volume of non-pegylated interferon alfa prescribed and dispensed in hospitals in England

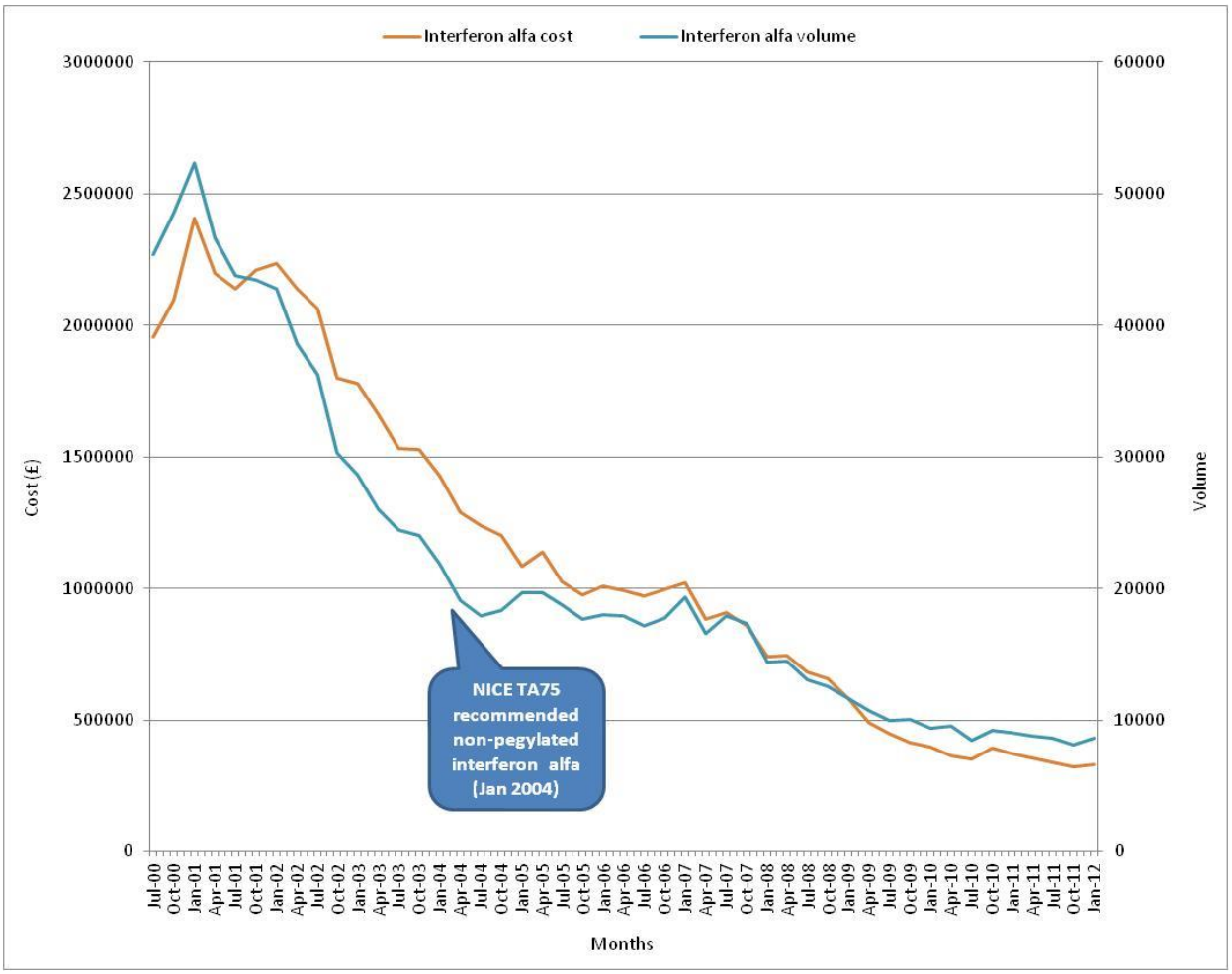
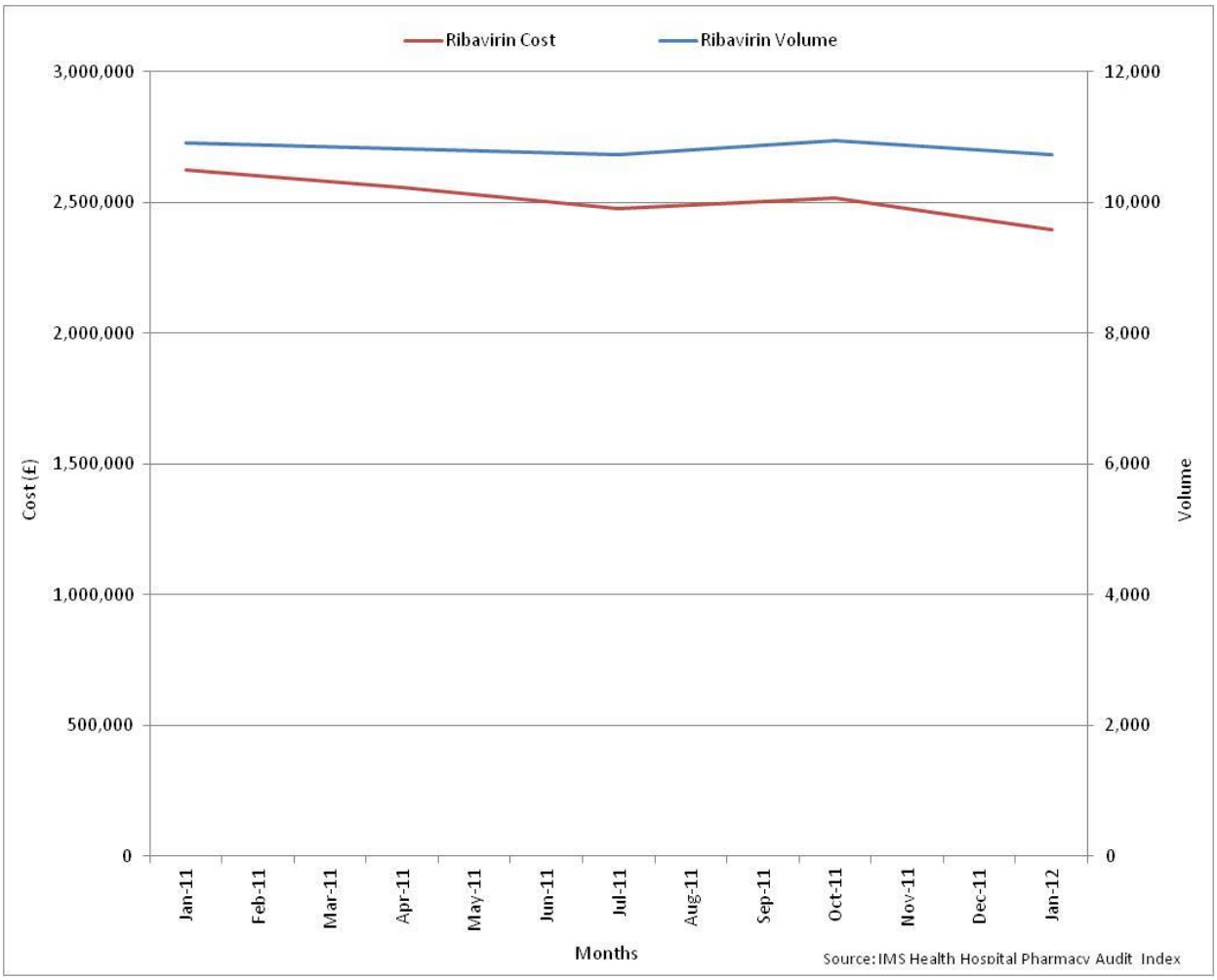


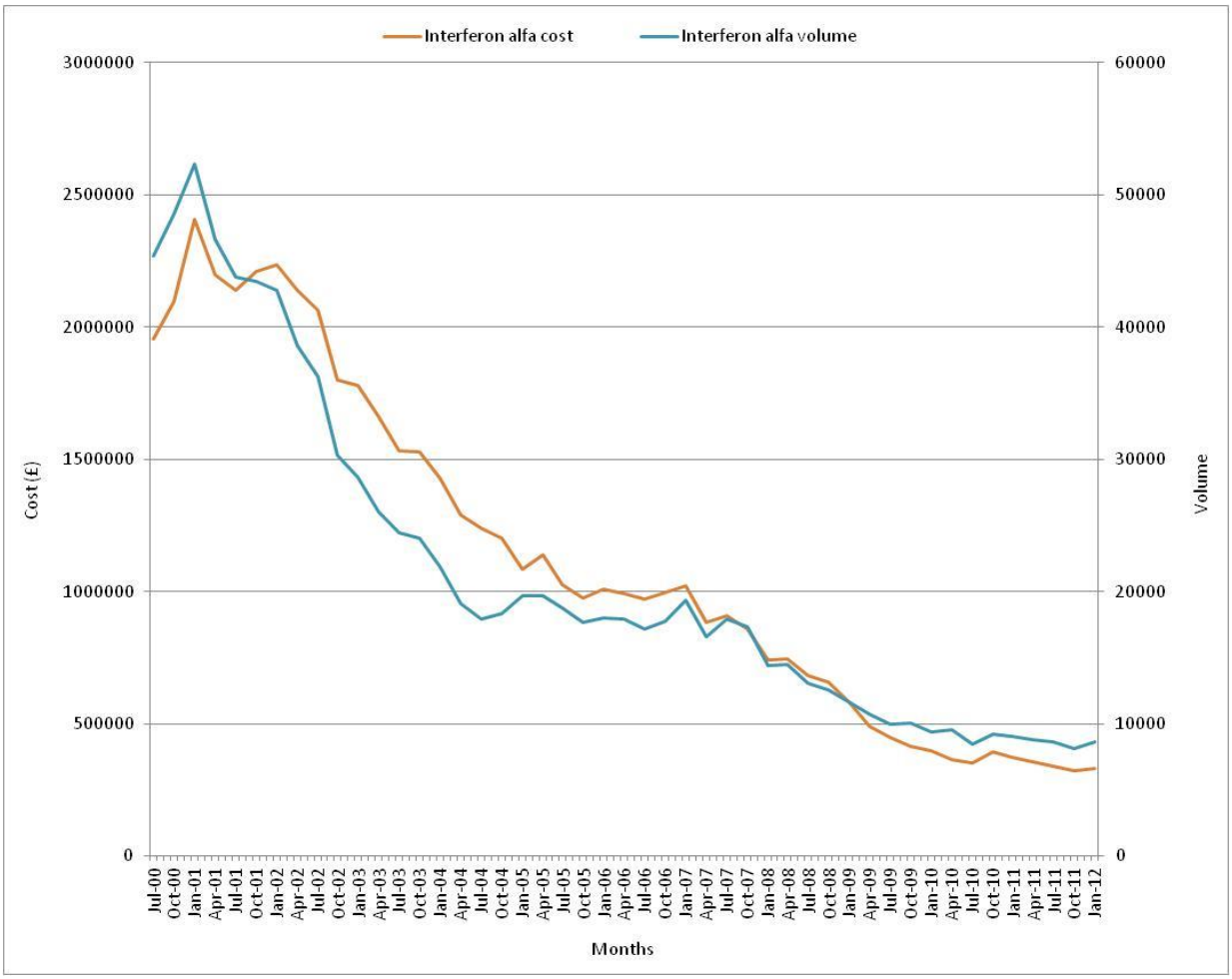
Figure 3 Cost and volume of ribavirin prescribed and dispensed in hospitals in England



1.2 ePACT data

This section presents net ingredient cost (NIC) and volume data of interferon alfa and pegylated interferon alfa, which has been prescribed and dispensed in primary care and hospitals and dispensed in the community in England.

Figure 5 Cost and volume of interferon alfa prescribed and dispensed in primary care and hospitals and dispensed in the community in England



2 Implementation studies from published literature

Information is taken from the uptake database (ERNIE) website.

2.1 Richards, M (2010) Extent and causes of international variation in drug usage: A report for the Secretary of State for Health by Professor Sir Mike Richards CBE

This report looks at medicines usage between countries, using IMS Health data. The WHO defined daily dose or the maximum or prescribed daily dose was used to measure usage. Results rank the UK relative to other countries usage and present calculations showing how close or otherwise the UK is to the average use across groups of other countries. It should be noted that countries other than the UK would

not be expected to adhere to NICE guidance making comparisons between countries not possible.

2.2 Health and Social Care Information Centre (2012) Use of NICE-appraised medicines in the NHS in England - 2010 and 2011, Experimental Statistics

This is the 3rd report published by the HSCIC on behalf of the DH to look at the variation in use of positively appraised medicines in relation to the expected use as predicted by NICE. In all, 52 medicines in 25 groups, relating to 35 technology appraisals were considered. Out of the 12 groups where a comparison could be made, observed use by the NHS in England was higher than the predicted use for 6 and lower for 6. For one drug group use was lower on one measure, and higher on another.

3 Qualitative input from the field team

The implementation field team have recorded the following feedback in relation to this guidance:

Nothing to add at this time

Appendix A: Healthcare activity data definitions

Prescribing analysis and cost tool system

This information comes from the electronic prescribing analysis and cost tool (ePACT) system, which covers prescriptions by GPs and non-medical prescribers in England and dispensed in the community in the UK. The Prescription Services Division of the NHS Business Services Authority maintains the system. PACT data are used widely in the NHS to monitor prescribing at a local and national level. Prescriptions dispensed in hospitals or mental health units, and private prescriptions, are not included in PACT data.

Measures of prescribing

Prescription Items: Prescriptions are written on a prescription form. Each single item written on the form is counted as a prescription item. The number of items is a measure of how many times the drug has been prescribed.

Cost: The net ingredient cost (NIC) is the basic price of a drug listed in the drug tariff, or if not in the drug tariff, the manufacturer's list price.

Data limitations (national prescriptions)

PACT data do not link to demographic data or information on patient diagnosis. Therefore the data cannot be used to provide prescribing information by age and sex or prescribing for specific conditions where the same drug is licensed for more than one indication.

IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

Measures of prescribing

Volume: The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

Data limitations

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for

prescribing of specific conditions where the same drug is licensed for more than one indication.