Technology Appraisal Guidance - No. 14

NHS

National Institute for Clinical Excellence

Guidance on the use of Ribavirin and Interferon Alpha for Hepatitis C

October 2000

This document has been circulated to the following:

- Health Authority Chief Executives in England and Wales
- NHS Trust Chief Executives in England and Wales
- PCG Chief Executives
- Local Health Group General Managers
- Medical and Nursing Directors
- All GP partners in England and Wales
- Consultant hepatologists and gastroenterologists in England and Wales
- Consultants in Infectious Diseases
- Chief Pharmacisists, Heads of Drug Purchasing, Heads of Drug Information, Pharmaceutical Advisors, GP Prescribing Advisors and Purchase Advisors in England and Wales
- NHS Director Wales
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- Chief Medical and Nursing Officers in England and Wales
- Medical Director & Head of NHS Quality – National Assembly for Wales
- Clinical Effectiveness Support Unit - Wales
- Representative bodies for health services, professional organisations and statutory bodies, Royal Colleges

This Guidance is written in the following context:
This guidance represents the view of the Institute's Appraisal Committee, the membership of which is set out in Appendix A, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgment about the use of Ribavirin and Interferon Alpha for Hepatitis C. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Guidance on the use of Ribavirin and Interferon Alpha for Hepatitis C

This section, Section 1, constitutes the Institute's Guidance on the Use of Ribavirin and Interferon Alpha for Hepatitis C. The remainder of the document is structured in the following way:

The full document and a summary of evidence will be available from our web site at www.nice.org.uk or by contacting 0541 555 455 and quoting reference number 00000.

Mae'r adran hon (adran 1) hefyd ar gael yn Gymraeg ar ein gwefan neu drwy gysylltu â 0541 555 455, rhif cyfeirnod, 0000.

1. Guidance

1.1. Interferon alpha and ribavirin as combination therapy is recommended for the treatment of moderate to severe hepatitis C (defined as histological evidence of significant scarring (fibrosis) and/or significant necrotic inflammation), at standard doses for patients over the age of 18 years as follows:-

1.1.1 All treatment-naïve patients (that is, those who have not previously had interferon alpha monotherapy or combination therapy) and all patients who have been treated with interferon alpha monotherapy, and have had some response but have since relapsed. Such treatment should be continued for 6 months for all patients.

1.1.2 A further 6 months combination therapy is recommended only for patients infected with hepatitis C virus of genotype 1, who respond to therapy by becoming clear of circulating viral RNA as detected by polymerase chain reaction (PCR) in the first 6 months.

1.1.3 Those in whom liver biopsy poses a substantially increased risk (such as patients with haemophilia) could be treated on clinical grounds without histology.

1.2 Therapy involving either or both of these drugs is not in general recommended for patients who are continuing intravenous drug users. Only where the prescribing clinician can be reliably assured that re-infection, compliance and drug interactions pose no problems should patients in this group be considered for combination therapy. Former intravenous drug users including those on oral maintenance therapy need not be excluded from therapy.

1.3 Therapy involving either or both of these drugs is not in general recommended for patients who are heavy users of alcohol, because of an increased risk of exacerbation of liver damage.

1.4 There is insufficient evidence for making recommendations on combination therapy for patients less than 18 years of age. There is also insufficient evidence for making recommendations for using combination therapy after liver transplantation.

1.5 Interferon alpha monotherapy should be considered only when ribavirin is contra-indicated or not tolerated. The recently licensed pegylated interferon monotherapy has not been considered in this guidance.

1.6 These recommendations are consistent with the European Association of the Study of the Liver (EASL) guidelines (see Appendix C) with the exception that (see para. 1.1.1), those who relapse after initially successful treatment by monotherapy are recommended for 6 months of combination therapy without the necessity of a viral load test after three months.

2 Clinical Need and Practice

2.1 Chronic hepatitis C is a disease of the liver caused by the hepatitis C virus (HCV). Six major genetic types of the hepatitis C virus have been found; these are of different virulence, and at least 40% are genotype 1; of the remainder the majority are genotypes 2 and 3. Generally the virus is transmitted parenterally but the natural history of the disease is not completely understood. It is acquired commonly through intravenous drug use and the sharing of needles. It was also spread through blood transfusion prior to the introduction of screening in 1991, as well as through blood products before the viral inactivation programme in the mid-1980s. There is a small risk of HCV infection associated with tattooing, electrolysis, ear piercing and acupuncture. Infection through sexual intercourse can also occur. There is a transmission rate of about 6% from mother to child if the mother is an HCV carrier. Concomitant HIV infection is thought to increase the risk of transmission.

2.2 After exposure to the virus, patients are often asymptomatic, however about 20% will develop acute hepatitis, some of whom will experience malaise, weakness and anorexia. Up to 85% of those exposed fail to clear the virus and go on to develop chronic hepatitis C. The ability of patients to rid themselves of the virus is partly related to the genotype of the virus, which affects the ability of the immune system to mount an effective response. The rate of progression of the disease is slow and variable, over 20-50 years. About 20-30% of those infected develop advanced liver disease or cirrhosis within 20 years and a small percentage of these develop hepatocellular carcinoma. A third of all those infected may never progress to cirrhosis or will not progress for at least 50 years. Patients with cirrhosis develop severe symptoms and complications. Patients with end stage liver disease or hepatocellular carcinoma may require liver transplantation.

2.3 Many individuals with HCV infection do not display symptoms. However, non-specific symptoms including fatigue, irritability, nausea, muscle ache, anorexia, abdominal discomfort, and right upper quadrant pain have been reported even in the absence of secondary pathology. If cirrhosis develops, patients may suffer severe symptoms and complications.

2.4 Estimates of prevalence for hepatitis C in England and Wales vary considerably, from 200,000 to 400,000. There is also great variation in prevalence between certain subgroups of the population: 0.04% in blood donors, 0.4% in antenatal attenders (in London), 1% in genito-urinary clinic attenders and up to 50% in intravenous drug users.

3 The Technology

3.1 The primary aims of treatment of patients with chronic hepatitis C are to achieve acceptable alanine aminotransferase (ALT) levels and clearance of hepatitis C virus (defined as undetectable HCV-RNA in the serum), with both sustained for at least 6 months after treatment cessation; in order to result in an improved quality of life for patients, a reduced risk of cirrhosis and hepatocellular carcinoma.

3.2 Until recently, interferon alpha was the only licensed treatment for chronic hepatitis C. The precise antiviral mode of action of interferon is unknown. However, it appears to alter host cell metabolism. There are several meta-analyses that review the effectiveness of interferon alpha in chronic hepatitis C. Approximately 47% of patients respond when treated with interferon alpha alone (monotherapy). More than half of these relapse within six months of stopping treatment. Treatment with interferon alpha is usually at the dose of 3 million units three times per week by subcutaneous injection. Injections may be administered by clinical staff or by the patient after adequate training. Patients who respond usually do so within three to four months, but some have had to continue with this dose of interferon alpha for 12 months.

3.3 Ribavirin (Rebetol, Schering-Plough) is currently licensed for use in combination with interferon alpha 2a (Roferon A, Hoffmann La Roche) and interferon alpha 2b (Viraferon, Schering Plough) for treatment of HCV in:

3.3.1 adult patients with histologically-proven, previously-untreated hepatitis C, without liver decompensation, who are positive for serum HCV-RNA and who have fibrosis or high inflammatory activity and

3.3.2 adult patients with chronic hepatitis C who have previously responded (with normalisation of ALT at the end of treatment) to interferon alpha but subsequently relapsed

3.4 Ribavirin is a nucleoside analogue with a broad spectrum of antiviral activity against RNA viruses. It is administered orally at a dose of either 1000mg (for patients weighing less than 75kg) per day, or 1200 mg (for patients weighing over 75kg), divided into 2 doses. Regular monitoring of full blood count to detect haemolytic anaemia is required in order to judge whether to reduce or cease ribavirin treatment.

3.5 Adverse effects related to combination therapy are similar in type and frequency to those of interferon alpha monotherapy and include influenza-like symptoms (fatigue, headache, fever), decreases in haematological parameters (anaemia, neutrophil count, white blood cell count, platelet), gastrointestinal complaints (anorexia, nausea), dermatological symptoms (alopecia), psychiatric disturbances (depression, anxiety) and hypo- or hyperthyroidism.

3.6 For patients considered for combination therapy, standard haematological tests and blood chemistry (i.e. full blood count and differential platelet count, liver function tests, uric acid, serum bilirubin and serum creatinine) are necessary for all patients before initiating therapy. Liver biopsy should be undertaken, where there are no increased risks, in order to assess liver scarring and necro-inflammation according to an

accepted severity scale such as the Knodell. This is important in determining the need for treatment in those with significant fibrosis and necro-inflammation. Patients should be seen weekly for the first four weeks, and then monthly for 6 months, to check for haemolysis and changes in thyroid activity. The genotype of the hepatitis C virus with which the patient is infected should also be determined for all candidates for combination therapy.

3.7 A four-week cycle of interferon alpha at 3 million units 3 times a week costs around £200, and four weeks of ribavirin costs about £550. Six months of combination therapy costs around £4800 (excluding monitoring, counselling and other infrastructure costs). Genotype testing, viral load measures and other pre-treatment services are estimated to cost a further £200 per patient.

3.8 In terms of other options for the treatment of chronic hepatitis C, a longer acting version of interferon alpha, pegylated interferon, is currently being evaluated in dose-ranging studies in combination with ribavirin. Preliminary results indicate that it has a similar tolerance profile to current combination therapy. A licence has been granted to Schering Plough by the EMEA for monotherapy with ViraferonPeg and a licence is currently pending to Hoffmann La Roche for monotherapy with Pegasys.

4 Evidence

4.1 *Clinical effectiveness*

4.1.1 In total, nineteen published RCTs involving 3765 patients and two meta analyses were identified that compared ribavirin and interferon alpha ('combination therapy') versus interferon alpha alone ('monotherapy').

4.1.2 Since it is not possible in the short term to measure directly the effectiveness of treatment in reducing progression to cirrhosis and hepatocellular carcinoma, three surrogate markers have been used in trials: hepatic histology; circulating virological loss of hepatitis C virus-RNA (by quantitative polymerase chain reaction (PCR)); and alanine aminotransferase (ALT) levels.

4.1.3 The single most useful factor in predicting effectiveness of combination therapy is viral genotype. Results from the pooling of two multicentre trials (involving 1744 individual patients) show that 67% of patients infected with hepatitis C virus (HCV) other than genotype 1 respond on a sustained basis to combination treatment within 24 weeks. There is no further gain from a further 24 weeks of treatment. Only 17% of those infected with HCV of genotype 1 respond on a sustained basis after 24 weeks of combination treatment; 28% have a sustained response after 48 weeks' treatment. Infection with genotypes 4, 5 and 6 is relatively rare in Britain, and therefore occurs infrequently in randomised trials.

4.1.4 Other patient factors which favour eradication of HCV are baseline viral load of less than 3.5 million copies/ml, favourable minimal hepatic histological abnormality on liver biopsy (i.e. no or minimal portal fibrosis), female gender, and age less than 40 years. However, no tests of interaction between these four factors or viral genotype appear to have been undertaken, so that any differential effect of combination therapy has not been addressed.

4.1.5 The effectiveness of combination therapy compared with monotherapy in patients being treated with interferon alpha for the first time, can be judged from the pooled results of two multicentre trials (see 4.1.3 above). The sustained virological responses rates were 33% (95% CI 29-37%) for patients on combination therapy compared with 6% (95% CI 3-10%) on monotherapy, based on 24 weeks treatment. The corresponding 48-week results were 41% (CI 36-45%) for combination therapy compared with 16% (CI 13-19%) for monotherapy. Biopsy and ALT results were consistent with a benefit of combination therapy in these patients.

4.1.6 The effectiveness of combination therapy in comparison with interferon monotherapy for relapsed patients (who responded to interferon alone but relapsed in the 6 months following initial treatment) was examined in a trial of 345 patients. Sustained virological response rates were 49% (95% CI 42-57%) on combination therapy compared with 5% (95% CI 2-9%) on monotherapy, for 24 weeks treatment. Biopsy and ALT results were consistent, with a benefit of combination therapy in relapsed patients.

4.1.7 The trials indicate that discontinuation of treatment (10-20%) is more frequent for combination therapy than for monotherapy. The most common reason either for study withdrawal or for dose reduction for combination therapy was related to haematological side effects. Treatment with combination therapy is frequently unpleasant and this may affect compliance.

4.1.8 Treatment of people who continue to use drugs intravenously is often not indicated due to the high probability of re-infection, presumed likelihood of relatively high levels of non-compliance and the possibility of drug interactions. Cessation of intravenous drug use before starting antiviral treatment is therefore important. Combination therapy is not contra-indicated for former intravenous drug users whose drug use has been stabilized on oral methadone or other products such as buprenorphine.

4.1.9 Evidence is currently lacking on the treatment of patients with mild/minimal changes on liver biopsy. The current consensus is that treatment is not necessary, though evidence as yet unpublished suggests that this strategy may need formal review.

4.1.10 Treatment of undecompensated cirrhosis with combination therapy appears to be much more successful than with monotherapy in which sustained response is very low. Treatment is more hazardous if the cirrhosis is decompensated and so is contra-indicated.

4.1.11 Evidence on whether non-responders to monotherapy respond to combination therapy is sparse and equivocal. Further research is necessary to determine whether it is either effective or cost-effective to treat this group.

4.2 *Cost effectiveness*

4.2.1 There have been a number of economic evaluations of the cost effectiveness of combination versus monotherapy.

4.2.2 For interferon alpha naïve patients, the incremental cost/QALY gained from treatment with combination therapy for 6 months in comparison with monotherapy has been estimated to be £7,000. For patients who have relapsed after a previous course of interferon alpha, the incremental discounted cost/QALY gained from 6 months of combination therapy compared with monotherapy has been estimated to be £3,050. Recent results comparing 6 months of combination therapy with 12 months of monotherapy show a cost per discounted QALY of about $US3,500 (£2,500) overall, the highest subclass figure being $US11,600 (£8,200) for genotype 1.

4.2.3 The incremental cost/QALY of treating for an additional six months (i.e. from 6 to 12 months) with combination therapy has been estimated to range from £5,000 to £36,000. Patients with genotype 1 who take longer to respond to treatment are a relatively cost-effective sub-group to treat for this additional period, but there is no additional benefit from the extra 6 months of treatment for genotypes 2 and 3. (While not all discounting of QALYs has been performed at the UK Treasury standard of 6% for costs and 1.5% for benefits, the effect is to make the estimates somewhat lower than appear above.)

5 Implications for the NHS

5.1 The total budget impact of combination therapy depends on a number of factors: prevalence, proportion of patients diagnosed, proportion of these who attend for assessment, and proportion considered suitable for treatment. If the prevalence

of chronic hepatitis C is 0.4%, if a quarter of these are diagnosed, if half of those diagnosed are under specialist care, if half of these have had a biopsy, and if a half of those biopsied are treated, then there will be about 7,000 patients in England and Wales treated in the first instance. Assuming that treatment of these patients is spread out over three years, that all receive 6 months' treatment and two-thirds receive 12 months' treatment, the drug cost would amount to about £55 million, or about £18 million per year. Testing (including viral genotyping), monitoring (including viral load tests) and counselling will need to be substantially increased above present levels, and their costs would be in addition to this sum. Moreover, as knowledge of the disease and its treatment becomes more widespread, it is also likely that more people than otherwise be diagnosed and will seek treatment. However, significant costs of treatment downstream from liver-related conditions, including transplantations, together with drug costs for those already on combination therapy, must be subtracted. In the longer run, when the "backlog" of cases from a number of years has been cleared, and assuming an incidence rate of 10% of the prevalence (i.e. 0.04%), the annual continuing drug cost would be about £5 million. However, it is most likely that rates of diagnosis, referral to specialists, biopsy and acceptance of the therapy will all increase, so this estimate of annual costs after three years is likely to be an underestimate.

5.2 The importance of ready access to appropriate health care infrastructure, including viral genotyping and other laboratory testing, and adequate counselling, particularly about the side effects of treatment, is recognised. Confidential HCV testing and counselling should be made available whether or not treatment is initiated.

5.3 While the recommended treatments should all be performed as a specialist activity in hospital, and therefore should have little implication for Primary Care workload, prescribing and budgets, it is nevertheless likely that there may be a transfer of activities to primary care, particularly in counselling, in which staff may require additional education and training.

6 Further Research

6.1 The prognostic value of monitoring viral load at one and three months with the aim of reducing the length of therapy for those patients whose viral load becomes undetectable should be investigated further.

6.2 Biopsy rates in diagnosed HCV carriers should be audited.

6.3 The largest single identifiable group of those infected with HCV is that of intravenous drug users. The majority of clinical trials performed on this technology have omitted this group of patients. Research related specifically to their treatment is therefore also needed.

6.4 Further research is also required to determine whether combination treatment of mild to moderate HCV patients and asymptomatic HCV carriers is clinically effective and cost-effective.

6.5 For patients who have not responded to interferon alpha monotherapy, research should be initiated to determine whether they respond to newer forms of therapy.

7 Implementation

7.1 As they reach the appropriate stage in their treatment patients should be offered the therapies set out in section 1 of this guidance

7.2 Physicians should review their practice in line with the guidance set out in section 1 of this guidance.

7.3 Trusts managing services in this area should review their facilities for viral genotyping with a view to upgrading and facilities for counselling will also need to be reviewed.

8 Clinical Audit Advice

8.1 To enable clinicians to audit their own compliance with this guidance it is recommended that treatment plans are recorded for each patient.

8.2 This information should be incorporated into local clinical audit data recording systems, and consideration given (if not already in place) to the establishment of appropriate categories in routine electronic record keeping systems used in hospitals and the multi-disciplinary groups working in this area.

8.3 Relevant clinical guidelines and protocols linking the multi-disciplinary groups working in this area should be reviewed in light of this guidance.

8.4 Prospective clinical audit programmes should record the proportion of treatments adhering to the guidance. Such programmes are likely to be more effective in improving patient care when they form part of the organisation's formal clinical governance arrangements and where they are linked to specific post-graduate activities.

9 Review of Guidance

9.1 This guidance will be reviewed in October 2003.

Andrew Dillon
Chief Executive

October 2000

APPENDIX A

Appraisal Committee Members

Professor R. L.Akehurst
Dean, School of Health Related Research
Sheffield University

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Professor of Clinical Pharmacology
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Mr James Partridge
Chief Executive
Changing Faces

Professor Philip Routledge
Professor of Clinical Pharmacology
University of Wales

Professor Andrew Stevens
Professor of Public Health
University of Birmingham

APPENDIX B

Sources of Evidence

The following documentation and opinion, on the use of ribavirin and interferon alpha for hepatitis C was made available to the Appraisal Committee:

a. Assessment Report

   Prepared by the Wessex Institute for Health Research and Development (Combination Therapy (Interferon Alfa and Ribavirin) in the treatment of Chronic Hepatitis C,June 2000)

b. Manufacturer/Sponsor submissions:

   1. Roche Products Ltd.
   2. Schering-Plough Ltd.

c. Professional/Specialist Group, Patient/carer Group and Trade Association submissions:

   1. British Association for the Study of the Liver
   2. British Liver Trust
   3. C Change
   4. Royal College of General Practitioners
   5. Royal College of Physicians and British Society of Gastroenterology - Guidelines
   6. The Haemophilia Society

d. The following experts were invited to make submissions to the committee:

   1. Professor Bassendine, Consultant Physician, Freeman Hospital, Newcastle-upon-Tyne
   2. Dr. Foster, Consultant Hepatologist, St.Mary's Hospital, London

APPENDIX C

EASL International Consensus Conference on Hepatitis C, Paris 26-8, Feb 1999 Consensus Statement, Journal of Hepatology 1999; 30: 956-61

APPENDIX D

Guidance on the use of Ribavirin and Interferon Alpha for Hepatitis C – Patient Information

The patient information in this appendix has been designed to support the production of your own information leaflets: you can download it from our web site (www.nice.org.uk) where it is available in English and Welsh. A printed version of this text is available in English/Welsh or English alone. If you would like copies of the printed leaflet please contact 0541 555 455, and quote the reference number 00000 for the English/Welsh version and 00000 for the English only version.

What is NICE Guidance?

The National Institute for Clinical Excellence (NICE) is a part of the NHS. It produces guidance for both the NHS and patients on medicines, medical equipment, diagnostic tests and clinical & surgical procedures and where they should be used.

When the Institute evaluates these things, it is called an appraisal. Each appraisal takes around 12 months to complete and involves the manufacturers of the drug or device, the professional organisations and the groups who represent patients.

NICE was asked to look at the available evidence on ribavirin and interferon alpha and provide guidance that would help the NHS in England and Wales decide where it should be used for Hepatitis C.

What is Hepatitis C?

Chronic hepatitis C is a disease of the liver caused by the hepatitis C virus. Six major types of the hepatitis C virus have been found, these are called genetic types (genotypes) and at least 4 out of 10 people who suffer from hepatitis C are infected with genotype 1. The virus is generally transmitted parenterally (this means by any means except digestion). Patients often get the virus through intravenous drug use and the sharing of needles. The virus was also spread through blood transfusion prior to the introduction of screening for the virus in 1991, as well as through blood products, such as factor 8 used by haemophiliacs, before the viral inactivation programme in the mid-1980s. There is a small risk of infection from tattooing, electrolysis, ear piercing and acupuncture. Infection through sexual intercourse can also occur, but again the risk is small and if a mother has the virus then there is a 6 in 100 chance she will pass it to her child. HIV infection is thought to increase the risk of transmission.

People exposed to the virus, often do not have any symptoms, however about 2 in 10 will quickly develop acute hepatitis. This is described as a short sharp illness and patients may feel weak and uncomfortable and lose their appetite, symptoms that have been described as flu-like with jaundice. 85 out of 100 people exposed to the virus go on to develop chronic hepatitis C. Development of the disease is slow and varies between people and can happen over 20-50 years. Of those infected 2 to 3 out of 10 people develop advanced liver disease (cirrhosis) within 20 years and a small number of these get cancer of the liver (hepatocellular carcinoma). People with advanced liver disease or cancer of the liver can develop severe symptoms and may require a liver transplant. A third of all people infected may never get cirrhosis or will not get it for at least 50 years

What is ribavirin/ interferon alpha?

Ribavirin and interferon alpha are drugs used to treat the Hepatitis C virus.

Interferon alpha can be used alone to treat people with the Hepatitis C virus. This is called monotherapy and about 47 out of 100 people with the virus respond to this treatment, but in more than half of those who respond to the treatment the infection returns within six months of stopping treatment. This treatment is given by an injection under the skin three times per week. Patients who respond to this treatment usually do so within three to four months, but some have had to continue with treatment for 12 months.

Ribavirin is a tablet that is currently licensed for use in combination with interferon alpha for the treatment of certain people with the hepatitis C virus. People taking ribavirin sometimes experience problem known as side effects therefore they should have regular blood tests in order to judge whether to reduce or stop ribavirin treatment. Patients should be seen weekly for the first four weeks of treatment, and then monthly for 6 months, to check for changes in the red blood cells and changes in the activity of the thyroid gland. The type of the hepatitis C virus should be determined for all people who are being considered for treatment with combination therapy as this can influence the treatment choice.

Results from clinical trials (involving 1744 individual patients) show that 67 out of 100 patients infected with hepatitis C virus (not genotype 1) respond to combination treatment within 24 weeks, this response is sustained and there is no gain from a further 24 weeks of treatment. If a patient is infected with hepatitis C that is genotype 1 then only 17 out of 100 respond on a sustained basis after 24 weeks of combination treatment; this increases to 28 out of 100 after 48 weeks' treatment.

What has NICE recommended about the use of ribavirin and interferon alpha?

1 In summary NICE has recommended to the NHS that the combination of interferon alpha and ribavirin should be used for the treatment of moderate to severe hepatitis C for the following patients over the age of 18 years: -

- All patients who have not previously been treated with interferon alpha (alone or in combination with another drug) and all patients who have previously been treated with interferon alpha monotherapy, and have had some response but have since relapsed. Such treatment should be continued for 6 months for all patients.

- A further 6 months combination therapy is recommended only for patients infected with a specific type of hepatitis C virus (genotype 1), who respond to the treatment in the first 6 months. Response is measured by the patient's blood becoming clear of a product of the Hepatitis C virus known as viral RNA. This is detected by a blood test called polymerase chain reaction, (PCR).

- A diagnosis of moderate to severe hepatitis C is made by taking a sample of cells from the liver (liver biopsy) and examining them under a microscope for evidence of liver

damage such as significant scarring (fibrosis) and/or significant inflammation. There are some people, such as those with haemophilia, for whom a liver biopsy may pose some risk and they can be treated without having to have a liver biopsy.

2 Treatment involving either or both of these drugs is not in general recommended for patients who are continuing intravenous drug users. Patients in this group should only be considered for combination therapy when the person prescribing treatment can be reliably assured that the patient will continue with the treatment as prescribed and that re-infection and drug interactions pose no problems. Former intravenous drug users including those who are taking oral drug substitutes can be offered this treatment for Hepatitis C.

3 Treatment involving ribavirin and interferon alpha (alone or together) is not generally recommended for people with Hepatitis C who are heavy users of alcohol, because of the risk of increasing liver damage.

4 There is not enough evidence to make recommendations on combination therapy for patients who are less than 18 years of age or for those who have had a liver transplant.

5 Treatment with Interferon alpha alone should be considered only when ribavirin is cannot be prescribed for medical reasons or where the patient experiences side effects that mean they cannot continue with treatment. The recently licensed pegylated interferon monotherapy is not been considered in this guidance.

What should I do?

If you, or someone you legally care for, has Hepatitis C then you can discuss this advice with your specialist or doctor at your next appointment.

Will NICE review its guidance?

Yes. The guidance will be reviewed in October 2003

Further Information

Further information on NICE, and the full guidance issued to the NHS is available on the NICE web site (www.nice.org.uk). It can also be requested from 0541 555 455, quoting reference [insert reference number].