UKMi North West

NICE Bites

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A summary of prescribing recommendations from NICE guidance

Chronic Hepatitis B

NICE CG165; 2013

This guideline covers the management of chronic hepatitis B in children, young people and adults.

Definition of terms

HBV	hepatitis B virus
HBsAg	hepatitis B surface antigen
HBeAg	hepatitis B e antigen
anti-HBc	antibody to hepatitis B core antigen
anti-HBs	antibody to hepatitis B surface antigen
ALT	alanine aminotransferase

Assessment and referral

Primary care

- Refer all people who are HBsAg positive to a paediatric or adult hepatologist or a gastroenterologist or infectious disease specialist with an interest in hepatology.
- Refer pregnant women who test HBsAg positive at antenatal screening within six weeks of results.
- Refer immediately to a hepatologist or gastroenterologist with an interest in hepatology, all adults who develop decompensated liver disease. Symptoms include ascites, encephalopathy and gastrointestinal haemorrhage.
- Arrange relevant tests and include results with the referral. See NICE Pathway

Secondary care

Adults

- Discuss the accuracy, limitations and risks of the different tests for liver disease with the patient.
- Ensure all healthcare professionals who refer adults for non-invasive tests are trained to interpret the results.
- Offer transient elastography as the initial test for liver disease in adults newly referred for assessment. For a transient elastography score:
  - ≥11 kPa: give antiviral treatment as per Box 1, without a liver biopsy.
  - 6 to 10 kPa: consider liver biopsy to confirm the level of fibrosis. Give antiviral treatment as per Box 1,
  - <6 kPa: offer liver biopsy to adults <30 years who have HBV DNA >2000 IU/ml and abnormal ALT** on two consecutive tests conducted three months apart. Give antiviral treatment as per Box 1.
- **Do NOT** offer liver biopsy to adults with a transient elastography score <6 kPa who have normal ALT and HBV DNA <2000 IU/ml as they are unlikely to have advanced liver disease or need antiviral treatment.
- Offer an annual reassessment using transient elastography to adults not taking antiviral treatment.

Children and young people

- Discuss the accuracy, limitations and risks of liver biopsy in determining the need for antiviral treatment with the child or young person and with parents/carers.
- Consider liver biopsy to assess liver disease and the need for antiviral treatment in children and young people with HBV DNA >2000 IU/ml and abnormal ALT** on two consecutive tests conducted 3 months apart. Offer biopsy under a general anaesthetic to children who are too young to tolerate the procedure under a local anaesthetic.

*See Summary of Product Characteristics for full prescribing information.

**Abnormal ALT: ≥30 IU/ml for males and ≥19 IU/ml for females.

Box 1

When to offer antiviral treatment - Adults

- Give antiviral treatment after consistent results from two consecutive tests conducted 3 months apart in adults:
  - ≥30 years who have HBV DNA >2000 IU/ml and abnormal ALT**,
  - <30 years who have HBV DNA >2000 IU/ml and abnormal ALT** if there is evidence of necroinflammation or fibrosis on liver biopsy or a transient elastography score >6 kPa,
  - who have HBV DNA >20,000 IU/ml and abnormal ALT** regardless of age or the extent of liver disease,
  - with cirrhosis and detectable HBV DNA, regardless of HBeAg status, HBV DNA and ALT levels.
- Consider antiviral treatment in adults with HBV DNA >2000 IU/ml and evidence of necroinflammation or fibrosis on liver biopsy.

Treatment and management

- Discuss treatment options, adverse effects and long-term prognosis before starting treatment.

Adults with HBeAg-positive chronic hepatitis B and compensated liver disease

First-line: a 48-week course of peginterferon alfa-2a*.

- After 24 weeks, consider stopping peginterferon alfa-2a* if HBV DNA level has decreased by <2 $\log_{10}$ IU/ml and/or if HBsAg is >20,000 IU/ml and give second-line treatment.

Second-line: give tenofovir disoproxil* to people who do not undergo HBeAg seroconversion or who relapse.

- Give entecavir*if tenofovir disoproxil* is contraindicated or not tolerated.
- Review adherence in people taking tenofovir disoproxil* who have detectable HBV DNA at 48 weeks:
  - if HBV DNA remains detectable at 96 weeks, and there is no history of lamivudine resistance, consider adding lamivudine* to tenofovir disoproxil*,
  - in people with a history of lamivudine resistance, consider adding entecavir* to tenofovir disoproxil*.
- Consider stopping treatment 12 months after HBeAg seroconversion in people without cirrhosis.
- **Do NOT** stop treatment in people with cirrhosis.

Adults with HBeAg-negative chronic hepatitis B and compensated liver disease

First-line: a 48-week course of peginterferon alfa-2a*.

- After 24 weeks, if HBV DNA level has decreased by <2 $\log_{10}$ IU/ml and HBsAg has not decreased, consider stopping peginterferon alfa-2a and give second-line treatment.

Second-line: give entecavir* or tenofovir disoproxil* to people with detectable HBV DNA after first-line treatment.

Third-line: consider switching from tenofovir disoproxil to entecavir or from entecavir to tenofovir disoproxil, in people who have detectable HBV DNA at 48 weeks.

- Consider stopping treatment 12 months after achieving undetectable HBV DNA and HBsAg seroconversion in people without cirrhosis.
- **Do NOT** stop treatment in people with cirrhosis.

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Adults with decompensated liver disease

- Manage in conjunction with a liver transplant centre.
- **Do NOT** give peginterferon alfa-2a*.

First-line: give entecavir* if there is no history of lamivudine resistance, **OR**

Second-line: give tenofovir disoproxil* to people with a history of lamivudine resistance.

- Reduce the dose of tenofovir disoproxil in people with renal impairment.

Children/young people with compensated liver disease

- Give antiviral treatment if there is evidence of significant fibrosis. See NICE Pathway.

First-line: consider a 48-week course of peginterferon alfa-2a**U**[c].

- Consider stopping after 24 weeks if HBV DNA level has decreased by <2 log10 IU/ml and/or HBsAg is >20,000 IU/ml.

Second-line: consider a nucleoside or nucleotide analogue e.g entecavir **U**[c], tenofovir disoproxil **U**[c] after first-line treatment if HBV DNA remains detectable.

Women who are pregnant or breastfeeding

- Discuss with pregnant women the benefits and risks of antiviral treatment for them and their baby.
- Avoid use of peginterferon alfa-2a* in pregnancy unless benefit outweighs risk. Women of childbearing potential must use effective contraception throughout therapy.
- Give tenofovir disoproxil***U** to women with HBV DNA >10^7 IU/ml in the third trimester to reduce risk of transmission of HBV to the baby.
- Monitor quantitative HBV DNA in the woman two months after starting tenofovir disoproxil and ALT monthly after the birth to detect postnatal HBV flares.
- Stop tenofovir disoproxil 4 to 12 weeks after the birth unless the mother meets criteria for long-term treatment.
- Offer active and passive hepatitis B immunisation to infants: see NICE Pathway
- Advise women there is no risk of transmitting HBV to their babies through breastfeeding if guidance on hepatitis B immunisation has been followed, and they may continue antiviral treatment whilst breastfeeding.

Adults co-infected with hepatitis C or hepatitis D

See NICE Pathway

Prophylaxis during immunosuppressive therapy

- Offer tests for anti-HBs, HBV DNA and ALT in people who are HBsAg and/or anti-HBc positive before starting immunosuppressive therapy for autoimmune or atopic diseases, chemotherapy, bone marrow or solid organ transplantation.
- In people who are HBsAg-positive and have HBV DNA >2000 IU/ml: give prophylaxis with entecavir*U or tenofovir disoproxil*U before starting immunosuppressive therapy and for a minimum of 6 months after HBeAg seroconversion and HBV DNA is undetectable.
- In people who are HBsAg-positive and have HBV DNA <2000 IU/ml:
  - consider lamivudine*U if immunosuppressive therapy is expected to last for <6 months. Monitor HBV DNA monthly and change to tenofovir disoproxil*U if HBV DNA remains detectable after 3 months,
  - consider entecavir*U or tenofovir disoproxil*U if immunosuppressive therapy is expected to last >6 months.
- In people who are HBsAg negative and anti-HBc positive and starting rituximab or other B cell-depleting therapies: give prophylaxis with lamivudine*U.
- In people who are HBsAg negative, anti-HBc positive and anti-HBs negative and not taking rituximab or other B cell-depleting therapies:
  - monitor HBV DNA monthly and offer prophylaxis to people whose HBV DNA becomes detectable,
  - consider lamivudine*U in people with HBV DNA <2000 IU/ml and for whom immunosuppressive therapy is expected to last <6 months; change to tenofovir disoproxil*U if HBV DNA remains detectable after 6 months,
  - consider entecavir*U or tenofovir disoproxil*U in people with HBV DNA >2000 IU/ml and for whom immunosuppressive therapy is expected to last >6 months.
- Start prophylaxis before beginning immunosuppressive therapy and continue for a minimum of 6 months after stopping immunosuppressive therapy.
- **Do NOT** offer prophylaxis to people who are HBsAg negative and anti-HBc and anti-HBs positive who are not taking rituximab or other B cell-depleting therapies.

Monitoring

- People **NOT** taking antiviral treatment and after treatment: see NICE Pathway

Peginterferon alfa-2a

- Review injection technique and adverse effects weekly during the first month of treatment.
- Monitor full blood count, liver, renal and thyroid function and in children, weight and height, before starting therapy and 2, 4,12, 24, 36 and 48 weeks during treatment to detect adverse effects.
- Monitor HBV DNA and quantitative HBsAg levels and HBeAg status before starting peginterferon alfa-2a and at 12, 24 and 48 weeks to determine treatment response.

Entecavir, lamivudine and tenofovir

Compensated liver disease

- Monitor full blood count, liver and renal function before starting treatment, after 4 weeks, then 3 monthly. In people starting tenofovir disoproxil, also monitor phosphate levels before starting treatment, at 4 weeks then 3 monthly.
- Monitor HBV DNA, quantitative HBsAg levels and HBeAg status before starting treatment then at 12, 24 and 48 weeks and then 6 monthly to determine treatment response and adherence.
- Monitor HBV DNA levels every 12 weeks in people with HBeAg negative disease who have been taking lamivudine for ≥5 years.

Decompensated liver disease

- Monitor full blood count, liver function, renal function, blood clotting, HBV DNA level and HBeAg status before starting treatment and weekly thereafter. In people starting tenofovir disoproxil, also monitor phosphate levels before starting treatment and weekly thereafter.
- When the person is no longer decompensated, follow recommendations for compensated liver disease.

See NICE Pathway: Hepatitis B

See NICE PH43: Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection

* See Summary of Product Characteristics for full prescribing information

U Unlicensed indication. Obtain and document informed consent.

U[c] Unlicensed for this indication in children/young people. Obtain and document informed consent.