NICE National Institute for Health and Care Excellence

NICE Pathways

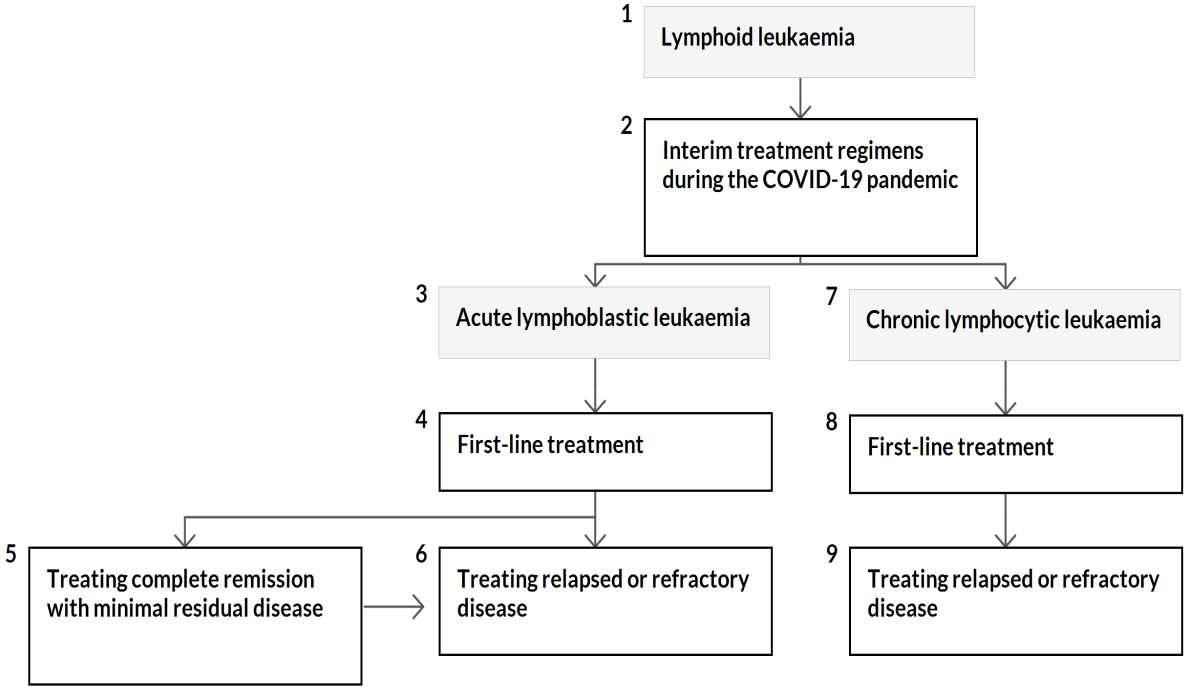
Lymphoid leukaemia

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:

http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
NICE Pathway last updated: 09 December 2020

This document contains a single flowchart and uses numbering to link the boxes to the associated recommendations.



1 Lymphoid leukaemia

No additional information

2 Interim treatment regimens during the COVID-19 pandemic

A table of NHS England interim treatment regimens gives possible alternative treatment options for use during the COVID-19 pandemic to reduce infection risk. This may affect decisions for people with cancer. See the COVID-19 rapid guideline: delivery of systemic anticancer treatments for more details.

3 Acute lymphoblastic leukaemia

No additional information

4 First-line treatment for acute lymphoblastic leukaemia

The following recommendations are from NICE technology appraisal guidance on pegaspargase for treating acute lymphoblastic leukaemia.

Pegaspargase, as part of antineoplastic combination therapy, is recommended as an option for treating acute lymphoblastic leukaemia in children, young people and adults only when they have untreated newly diagnosed disease.

This guidance is not intended to affect the position of patients whose treatment with pegaspargase was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop. For children and young people, this decision should be made jointly by the clinician and the child or young person, or the child or young person's parents or carers.

NICE has written information for the public on pegaspargase.

5 Treating complete remission with minimal residual disease

The following recommendations are from NICE technology appraisal guidance on blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity.

Blinatumomab is recommended as an option for treating Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia in adults with minimal residual disease (MRD) of at least 0.1%, only if:

- the disease is in first complete remission and
- the company provides blinatumomab according to the commercial arrangement.

This recommendation is not intended to affect treatment with blinatumomab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

See why we made these recommendations on blinatumomab.

NICE has written information for the public on blinatumomab.

6 Treating relapsed or refractory acute lymphoblastic leukaemia

Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years

The following recommendations are from NICE technology appraisal guidance on tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years.

Tisagenlecleucel therapy is recommended for use within the Cancer Drugs Fund as an option for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years, only if the conditions in the managed access agreement are followed.

This recommendation is not intended to affect both treatment in preparation for and treatment with tisagenlecleucel that was started in the NHS before this guidance was published. People

having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. For young people aged under 18 years, this decision should be made jointly by the clinician and the young person, or the young person's parents or carers.

See why we made these recommendations on tisagenlecleucel.

NICE has written information for the public on tisagenlecleucel.

Inotuzumab ozogamicin

The following recommendations are from NICE technology appraisal guidance on inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia.

Inotuzumab ozogamicin is recommended, within its marketing authorisation, as an option for treating relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia in adults. People with relapsed or refractory Philadelphia-chromosome-positive disease should have had at least 1 tyrosine kinase inhibitor.

Inotuzumab ozogamicin is recommended only if the company provides it according to the commercial arrangement.

See why we made the recommendations on inotuzumab ozogamicin [See page 15].

NICE has written information for the public on inotuzumab ozogamicin.

Blinatumomab

The following recommendation is from NICE technology appraisal guidance on blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia.

Blinatumomab is recommended within its marketing authorisation as an option for treating Philadelphia-chromosome-negative relapsed or refractory precursor B-cell acute lymphoblastic leukaemia in adults, only if the company provides it with the discount agreed in the patient access scheme.

NICE has written information for the public on blinatumomab.

Ponatinib

The following recommendations are an extract from NICE technology appraisal guidance on ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia.

Ponatinib is recommended, within its marketing authorisation, as an option for treating Philadelphia-chromosome-positive acute lymphoblastic leukaemia in adults when:

- the disease is resistant to dasatinib or
- they cannot tolerate dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate or
- the T315I gene mutation is present.

Ponatinib is recommended only if the company provides the drug with the discount agreed in the patient access scheme.

NICE has written information for the public on ponatinib.

7 Chronic lymphocytic leukaemia

No additional information

8 First-line treatment for chronic lymphocytic leukaemia

Venetoclax with obinutuzumab

The following recommendations are from NICE technology appraisal guidance on venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia.

Venetoclax plus obinutuzumab is recommended as an option for untreated CLL in adults, only if:

- there is a 17p deletion or TP53 mutation, or
- there is no 17p deletion or TP53 mutation, and fludarabine plus cyclophosphamide and rituximab (FCR), or bendamustine plus rituximab (BR), is unsuitable, and
- the companies provide the drugs according to the commercial arrangements.

Venetoclax plus obinutuzumab is recommended for use within the Cancer Drugs Fund as an option for untreated CLL in adults, only if:

- there is no 17p deletion or TP53 mutation, and FCR or BR is suitable, and

- the conditions in the managed access agreement for venetoclax plus obinutuzumab are followed.

These recommendations are not intended to affect treatment with venetoclax plus obinutuzumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

See why we made the recommendations on venetoclax with obinutuzumab.

NICE has written information for the public on venetoclax with obinutuzumab.

Venetoclax

The following recommendations are an extract from NICE technology appraisal guidance on venetoclax for treating chronic lymphocytic leukaemia.

Venetoclax is recommended for use within the Cancer Drugs Fund, within its marketing authorisation, as an option for treating chronic lymphocytic leukaemia, that is in adults:

- with a 17p deletion or TP53 mutation and when a B-cell receptor pathway inhibitor is unsuitable and
- only if the conditions in the managed access agreement are followed.

This recommendation is not intended to affect treatment with venetoclax that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on venetoclax.

Ibrutinib

17p deletion or TP53 mutation

The following recommendation is an extract from NICE technology appraisal guidance on ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation.

Ibrutinib alone is recommended within its marketing authorisation as an option for treating

chronic lymphocytic leukaemia in adults who have a 17p deletion or TP53 mutation and in whom chemo-immunotherapy is unsuitable, only when the company provides ibrutinib with the discount agreed in the patient access scheme.

NICE has written information for the public on ibrutinib.

Without 17p deletion or TP53 mutation

NICE is unable to make a recommendation about the use in the NHS of ibrutinib for untreated chronic lymphocytic leukaemia without a 17p deletion or TP53 mutation because no evidence submission was received from Janssen-Cilag. The company has confirmed that it does not intend to make a submission.

Idelalisib

September 2016: The European Medicines Agency has reviewed idelalisib and the marketing authorisation has been updated.

For people taking idelalisib as a first therapy, the marketing authorisation now states that idelalisib is for 'first-line treatment in the presence of 17p deletion or TP53 mutation in patients who are not eligible for any other therapies'.

Additional information about infections has been included in the marketing authorisation.

Idelalisib with rituximab

The following recommendations are from NICE technology appraisal guidance on idelalisib for treating chronic lymphocytic leukaemia.

Idelalisib, in combination with rituximab, is recommended for untreated chronic lymphocytic leukaemia in adults with a 17p deletion or TP53 mutation.

Idelalisib is recommended only if the company provides the drug with the discount agreed in the simple discount agreement.

People whose treatment with idelalisib is not recommended in this NICE guidance but was started within the NHS before this guidance was published should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on idelalisib.

Idelalisib with ofatumumab

The NICE technology appraisal of idelalisib with ofatumumab for treating chronic lymphocytic leukaemia was terminated because no evidence submission was received from Gilead Sciences for the technology. The company has confirmed that it does not intend to make a submission. Therefore NICE was unable to make a recommendation about the use of this technology in the NHS, but will review this decision if the company decides to make a submission.

Obinutuzumab

The following recommendations are from NICE technology appraisal guidance on obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia.

Obinutuzumab, in combination with chlorambucil, is recommended as an option for adults with untreated chronic lymphocytic leukaemia who have comorbidities that make full-dose fludarabine-based therapy unsuitable for them, only if:

- bendamustine-based therapy is not suitable and
- the company provides obinutuzumab with the discount agreed in the patient access scheme.

People whose treatment with obinutuzumab is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on obinutuzumab.

Bendamustine

The following recommendation is from NICE technology appraisal guidance on bendamustine for the first-line treatment of chronic lymphocytic leukaemia.

Bendamustine is recommended as an option for the first-line treatment of chronic lymphocytic leukaemia (Binet stage B or C) in patients for whom fludarabine combination chemotherapy is not appropriate.

NICE has written information for the public on first-line bendamustine.

Rituximab

The following recommendation is from NICE technology appraisal guidance on rituximab for the first-line treatment of chronic lymphocytic leukaemia.

Rituximab in combination with fludarabine and cyclophosphamide is recommended as an option for the first-line treatment of chronic lymphocytic leukaemia in people for whom fludarabine in combination with cyclophosphamide is considered appropriate.

Rituximab in combination with chemotherapy agents other than fludarabine and cyclophosphamide is not recommended for the first-line treatment of chronic lymphocytic leukaemia.

NICE has written information for the public on first-line rituximab.

Fludarabine

The following recommendation is from NICE technology appraisal guidance on fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia.

Fludarabine monotherapy, within its licensed indication, is not recommended for the first-line treatment of chronic lymphocytic leukaemia.

NICE has written information for the public on fludarabine monotherapy.

9 Treating relapsed or refractory chronic lymphocytic leukaemia

Venetoclax

Venetoclax with rituximab

The following recommendation is from NICE technology appraisal guidance on venetoclax with rituximab for previously treated chronic lymphocytic leukaemia.

Venetoclax with rituximab is recommended, within its marketing authorisation, as an option for treating chronic lymphocytic leukaemia in adults who have had at least 1 previous therapy. It is recommended only if the company provides it according to the commercial arrangement.

See why we made the recommendation on venetoclax with rituximab.

NICE has written information for the public on venetoclax with rituximab.

Venetoclax monotherapy

The following recommendations are an extract from NICE technology appraisal guidance on venetoclax for treating chronic lymphocytic leukaemia.

Venetoclax is recommended for use within the Cancer Drugs Fund, within its marketing authorisation, as an option for treating chronic lymphocytic leukaemia, that is in adults:

- with a 17p deletion or TP53 mutation and whose disease has progressed after a B-cell receptor pathway inhibitor or
- without a 17p deletion or TP53 mutation, and whose disease has progressed after both chemo-immunotherapy and a B-cell receptor pathway inhibitor and
- only if the conditions in the managed access agreement are followed.

This recommendation is not intended to affect treatment with venetoclax that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on venetoclax monotherapy.

Ibrutinib

Ibrutinib with bendamustine and rituximab

The appraisal of ibrutinib with bendamustine and rituximab for treating relapsed or refractory chronic lymphocytic leukaemia after systemic therapy was terminated because no evidence submission was received from the manufacturer or sponsor of the technology. Therefore NICE is unable to make a recommendation about the use in the NHS of ibrutinib with bendamustine and rituximab for treating relapsed or refractory chronic lymphocytic leukaemia after systemic therapy.

Ibrutinib monotherapy

The following recommendation is an extract from NICE technology appraisal guidance on ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation.

Ibrutinib alone is recommended within its marketing authorisation as an option for treating

chronic lymphocytic leukaemia in adults who have had at least 1 prior therapy, only when the company provides ibrutinib with the discount agreed in the patient access scheme.

NICE has written information for the public on ibrutinib monotherapy.

Idelalisib

Idelalisib with rituximab

The following recommendations are from NICE technology appraisal guidance on idelalisib for treating chronic lymphocytic leukaemia.

Idelalisib, in combination with rituximab, is recommended for chronic lymphocytic leukaemia in adults when the disease has been treated but has relapsed within 24 months.

Idelalisib is recommended only if the company provides the drug with the discount agreed in the simple discount agreement.

People whose treatment with idelalisib is not recommended in this NICE guidance but was started within the NHS before this guidance was published should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on idelalisib.

Idelalisib with ofatumumab

The NICE technology appraisal of idelalisib with ofatumumab for treating chronic lymphocytic leukaemia was terminated because no evidence submission was received from Gilead Sciences for the technology. The company has confirmed that it does not intend to make a submission. Therefore NICE was unable to make a recommendation about the use of this technology in the NHS, but will review this decision if the company decides to make a submission.

Rituximab

The following recommendations are from NICE technology appraisal guidance on rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia.

Rituximab in combination with fludarabine and cyclophosphamide is recommended as a treatment option for people with relapsed or refractory chronic lymphocytic leukaemia except

when the condition:

- is refractory to fludarabine (that is, it has not responded to fludarabine or has relapsed within 6 months of treatment) or
- has previously been treated with rituximab, unless:
  - in the context of a clinical trial, at a dose lower than the dose currently licensed for chronic lymphocytic leukaemia or
  - in the context of a clinical trial, in combination with chemotherapy other than fludarabine and cyclophosphamide.

Rituximab in combination with fludarabine and cyclophosphamide is recommended only in the context of research for people with relapsed or refractory chronic lymphocytic leukaemia that has previously been treated with rituximab, unless rituximab has been given as specified above.

Rituximab in combination with chemotherapy other than fludarabine and cyclophosphamide is recommended only in the context of research for people with relapsed or refractory chronic lymphocytic leukaemia.

People with chronic lymphocytic leukaemia that is refractory to fludarabine (as defined in the first paragraph and bullet points above), who are currently receiving rituximab in combination with fludarabine and cyclophosphamide should have the option to continue treatment until they and their clinicians consider it appropriate to stop.

People with chronic lymphocytic leukaemia that has previously been treated with rituximab (other than as specified in the first paragraph and bullet points above), who are currently receiving rituximab in combination with fludarabine and cyclophosphamide and people who are currently receiving rituximab in combination with other chemotherapy regimens that is not in the context of research, should have the option to continue treatment until they and their clinicians consider it appropriate to stop.

NICE has written information for the public on rituximab for relapsed or refractory chronic lymphocytic leukaemia.

Fludarabine

The following recommendations are from (NICE technology appraisal guidance on the use of fludarabine for B-cell chronic lymphocytic leukaemia.

Oral fludarabine is recommended as second line therapy for B-cell chronic lymphocytic leukaemia (CLL) for patients who have either failed, or are intolerant of, first line chemotherapy,

and who would otherwise have received combination chemotherapy of either:

- cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP)
- cyclophosphamide, doxorubicin and prednisolone (CAP) or
- cyclophosphamide, vincristine and prednisolone (CVP).

The oral formulation of fludarabine is preferred to the intravenous formulation on the basis of more favourable cost effectiveness. Intravenous fludarabine should only be used when oral fludarabine is contra-indicated.

NICE has written information for the public on second-line fludarabine.

Rationale: inotuzumab ozogamicin

Treatment for relapsed or refractory B-cell acute lymphoblastic leukaemia is usually fludarabine, cytarabine and granulocyte colony-stimulating factor based chemotherapy (FLAG) with idarubicin. People with Philadelphia-chromosome-positive disease can have FLAG-based therapy with tyrosine kinase inhibitors or tyrosine kinase inhibitors alone. Clinical trial evidence does not show an overall survival benefit for people having inotuzumab ozogamicin compared with those having FLAG, high-dose cytarabine or cytarabine with mitoxantrone-based chemotherapy. However, more people having inotuzumab ozogamicin are able to go on to have a stem cell transplant when compared with people having the other treatments. Inotuzumab ozogamicin also meets NICE's criteria to be a life-extending treatment at the end of life.

The most plausible cost-effectiveness estimates for inotuzumab ozogamicin compared with standard care are in the range NICE considers an acceptable use of NHS resources. Therefore it can be recommended for treating relapsed or refractory B-cell acute lymphoblastic leukaemia.

For more information see the committee discussion in the NICE technology appraisal guidance on inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia.

Glossary

CLL

chronic lymphocytic leukaemia

Sources

Venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia (2020) NICE technology appraisal guidance 663

Blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity (2019) NICE technology appraisal guidance 589

Venetoclax with rituximab for previously treated chronic lymphocytic leukaemia (2019) NICE technology appraisal guidance 561

Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years (2018) NICE technology appraisal guidance 554

Inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia (2018) NICE technology appraisal guidance 541

Venetoclax for treating chronic lymphocytic leukaemia (2017) NICE technology appraisal guidance 487

Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia (2017) NICE technology appraisal guidance 451

Blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia (2017) NICE technology appraisal guidance 450

Ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation (2017) NICE technology appraisal guidance 429

Pegaspargase for treating acute lymphoblastic leukaemia (2016) NICE technology appraisal guidance 408

Idelalisib for treating chronic lymphocytic leukaemia (2015) NICE technology appraisal guidance 359

Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia (2015) NICE technology appraisal guidance 343

Bendamustine for the first-line treatment of chronic lymphocytic leukaemia (2011) NICE technology appraisal guidance 216

Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (2010) NICE technology appraisal guidance 193

Rituximab for the first-line treatment of chronic lymphocytic leukaemia (2009) NICE technology appraisal guidance 174

Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia (2007) NICE technology appraisal guidance 119

Guidance on the use of fludarabine for B-cell chronic lymphocytic leukaemia (2001) NICE technology appraisal guidance 29

Your responsibility

Guidelines

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Technology appraisals

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take these recommendations fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this interactive flowchart is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the recommendations to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to

have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Medical technologies guidance, diagnostics guidance and interventional procedures guidance

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take these recommendations fully into account. However, the interactive flowchart does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the recommendations, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this interactive flowchart should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.