NICE National Institute for Health and Care Excellence

NICE Pathways

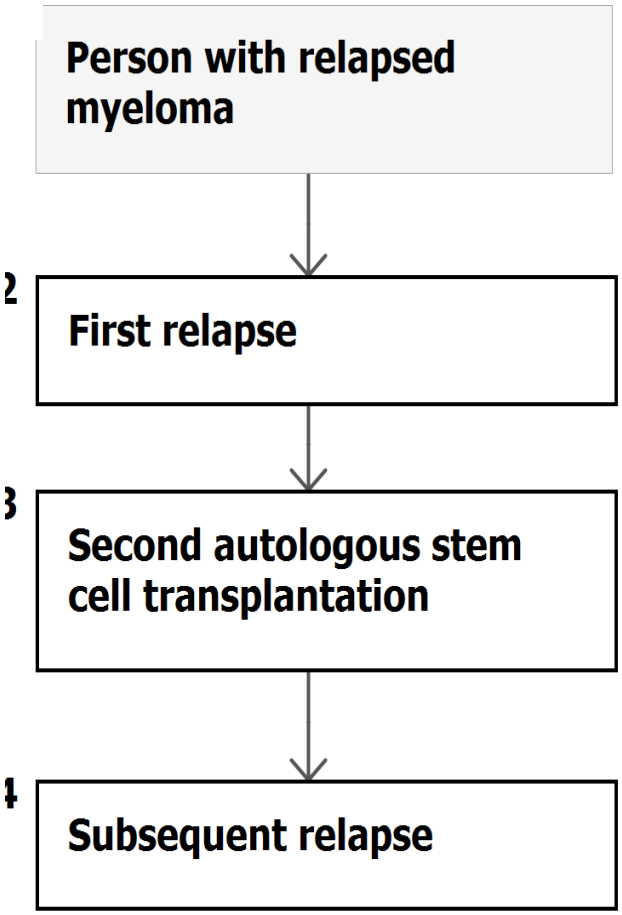
Managing relapse of myeloma

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/myeloma
NICE Pathway last updated: 09 April 2019

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



1 Person with relapsed myeloma

No additional information

2 First relapse

Daratumumab with bortezomib and dexamethasone

The following recommendations are from NICE technology appraisal guidance on daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma.

Daratumumab plus bortezomib plus dexamethasone is recommended for use within the Cancer Drugs Fund as an option for treating relapsed multiple myeloma in people who have had 1 previous treatment. It is recommended only if the conditions in the managed access agreement for daratumumab plus bortezomib plus dexamethasone are followed.

This recommendation is not intended to affect treatment with daratumumab plus bortezomib plus dexamethasone 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 the recommendations on daratumumab with bortezomib and dexamethasone

NICE has written information for the public on daratumumab with bortezomib and dexamethasone.

Carfilzomib

The following recommendations are from NICE technology appraisal guidance on carfilzomib for previously treated multiple myeloma.

Carfilzomib in combination with dexamethasone is recommended as an option for treating multiple myeloma in adults, only if:

- they have had only 1 previous therapy, which did not include bortezomib and
- the company provides carfilzomib with the discount agreed in the patient access scheme.

These recommendations are not intended to affect treatment with carfilzomib 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.

NICE has written information for the public on carfilzomib.

Bortezomib

The following recommendations are from NICE technology appraisal guidance on bortezomib monotherapy for relapsed multiple myeloma.

Bortezomib monotherapy is recommended as an option for the treatment of progressive multiple myeloma in people who are at first relapse having received one prior therapy and who have undergone, or are unsuitable for, bone marrow transplantation, under the following circumstances:

- the response to bortezomib is measured using serum M protein after a maximum of four cycles of treatment, and treatment is continued only in people who have a complete or partial response (that is, reduction in serum M protein of 50% or more or, where serum M protein is not measurable, an appropriate alternative biochemical measure of response) **and**
- the manufacturer rebates the full cost of bortezomib for people who, after a maximum of four cycles of treatment, have less than a partial response (as defined above).

People currently receiving bortezomib monotherapy who do not meet the criteria above should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

NICE has written information for the public on bortezomib monotherapy.

3 Second autologous stem cell transplantation

Offer second autologous stem cell transplantation to people with relapsed myeloma who are suitable and who have:

- completed re-induction therapy without disease progression and
- had a response duration of more than 24 months after their first autologous stem cell transplant.

Consider second autologous stem cell transplantation for people with relapsed myeloma who

are suitable and who have:

- completed reinduction therapy without disease progression and
- had a response duration of between 12 and 24 months after their first autologous stem cell transplant.

Be aware that people with relapsed myeloma are more likely to be suitable for a second autologous stem cell transplantation, if they have:

- had a good response to the first autologous stem cell transplant
- a lower ISS stage
- not had many prior treatments
- good overall fitness, based on resilience, frailty and performance status
- no adverse FISH results.

4 Subsequent relapse

Ixazomib

The following recommendations are from NICE technology appraisal guidance on ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma.

Ixazomib, with lenalidomide and dexamethasone, is recommended for use within the Cancer Drugs Fund as an option for treating multiple myeloma in adults only if:

- they have already had 2 or 3 lines of therapy and
- the conditions in the managed access agreement for ixazomib are followed.

This recommendation is not intended to affect treatment with ixazomib 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 the recommendations on ixazomib [See page 9].

NICE has written information for the public on ixazomib.

Lenalidomide

The following recommendations are from NICE technology appraisal guidance on lenalidomide

for the treatment of multiple myeloma in people who have received at least one prior therapy.

Lenalidomide in combination with dexamethasone is recommended, within its licensed indication, as an option for the treatment of multiple myeloma only in people who have received two or more prior therapies, with the following condition:

- The drug cost of lenalidomide (excluding any related costs) for people who remain on treatment for more than 26 cycles (each of 28 days; normally a period of 2 years) will be met by the manufacturer.

People currently receiving lenalidomide for the treatment of multiple myeloma, but who have not received two or more prior therapies, should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

NICE has written information for the public on lenalidomide.

Panobinostat

The following recommendations are from NICE technology appraisal guidance on panobinostat for treating multiple myeloma after at least 2 previous treatments.

Panobinostat in combination with bortezomib and dexamethasone is recommended, within its marketing authorisation, as an option for treating multiple myeloma, that is, for 'adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent' when the company provides panobinostat with the discount agreed in the patient access scheme.

NICE has written information for the public on panobinostat.

Daratumumab

The following recommendations are from NICE technology appraisal guidance on daratumumab monotherapy for treating relapsed and refractory multiple myeloma.

Daratumumab monotherapy is recommended for use within the Cancer Drugs Fund as an option for treating relapsed and refractory multiple myeloma in adults whose previous therapy included a proteasome inhibitor and an immunomodulator, and whose disease progressed on the last therapy, only if:

- they have daratumumab after 3 previous therapies and
- the conditions in the managed access agreement are followed.

This recommendation is not intended to affect treatment with daratumumab 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 daratumumab monotherapy.

NICE is unable to make a recommendation about the use in the NHS of daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma because no evidence submission was received from Janssen-Cilag. The company has confirmed that it does not intend to make a submission.

Pomalidomide

The following recommendations are from NICE technology appraisal guidance on pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib.

Pomalidomide, in combination with low-dose dexamethasone, is recommended as an option for treating multiple myeloma in adults at third or subsequent relapse; that is, after 3 previous treatments including both lenalidomide and bortezomib, only when the company provides pomalidomide with the discount agreed in the patient access scheme.

This guidance is not intended to affect the position of patients whose treatment with pomalidomide 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.

NICE has written information for the public on pomalidomide.

Bortezomib

NICE is unable to make a recommendation about the use in the NHS of bortezomib for treating multiple myeloma after second or subsequent relapse because no evidence submission was received from Janssen-Cilag. The company has confirmed that it does not intend to make a submission.

Elotuzumab

The NICE technology appraisal of elotuzumab for previously treated multiple myeloma was terminated because no evidence submission was received from Bristol–Myers Squibb for the technology. Therefore NICE **was unable to make a recommendation** about the use in the NHS of elotuzumab for previously treated multiple myeloma, but will review this decision if the company decides to make a submission.

Why we made the recommendations on ixazomib

Ixazomib, with lenalidomide and dexamethasone, has a marketing authorisation to treat multiple myeloma in people who have already had 1 or more lines of therapy. But it is likely to be used only for people who have already had 2 or 3 lines of therapy, for whom current treatment is lenalidomide plus dexamethasone, so the appraisal focused on this population.

The main clinical trial is ongoing. For people who have already had 2 or 3 lines of therapy, ixazomib (with lenalidomide and dexamethasone) increases the length of time they live without their disease progressing, when compared with lenalidomide plus dexamethasone alone. It is not yet clear whether ixazomib (with lenalidomide plus dexamethasone) prolongs life compared with lenalidomide plus dexamethasone alone, but the initial results are promising.

Ixazomib does not meet NICE's criteria to be considered a life-extending treatment at the end of life.

Ixazomib has the potential to be cost effective for people who have had 2 or 3 lines of therapy, at the price agreed in a commercial access agreement as part of the managed access agreement. But more evidence is needed to address the clinical uncertainties. It can therefore be recommended for use within the Cancer Drugs Fund while further data are collected from the clinical trial, and through the Systemic Anti-Cancer Therapy dataset.

For more information see the committee discussion in the NICE technology appraisal guidance on ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma.

Glossary

FDG PET-CT

fluorodeoxyglucose positron emission tomography CT

FISH

fluorescence in-situ hybridisation

GvHD

graft-versus-host disease

HLA

human leukocyte antigen

INR

international normalised ratio

ISS

international Staging System

LMWH

low molecular weight heparin

MDT

multidisciplinary team

MDTs

multidisciplinary teams

MGUS

monoclonal gammopathy of undetermined significance

smouldering myeloma

(asymptomatic myeloma which has no evidence of myeloma-related organ or tissue injury or a myeloma defining event)

Sources

Myeloma: diagnosis and management (2016) NICE guideline NG35

Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (2019) NICE technology appraisal guidance 573

Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2018) NICE technology appraisal guidance 510

Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2018) NICE technology appraisal guidance 505

Carfilzomib for previously treated multiple myeloma (2017) NICE technology appraisal guidance 457

Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2017) NICE technology appraisal 454

Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal) (2017) NICE technology appraisal 453

Elotuzumab for previously treated multiple myeloma (terminated appraisal) (2017) NICE technology appraisal 434

Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427

Panobinostat for treating multiple myeloma after at least 2 previous treatments (2016) NICE technology appraisal guidance 380

Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (2009) NICE technology appraisal guidance 171

Bortezomib monotherapy for relapsed multiple myeloma (2007) NICE technology appraisal guidance 129

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.