

**NATIONAL INSTITUTE FOR HEALTH AND CARE  
EXCELLENCE**

**Final appraisal determination**

**Obinutuzumab with bendamustine for treating  
follicular lymphoma refractory to rituximab**

This guidance was developed using the single technology appraisal (STA) process.

**1 Guidance**

- 1.1 Obinutuzumab in combination with bendamustine followed by obinutuzumab maintenance is recommended for use within the Cancer Drugs Fund as an option for treating follicular lymphoma that did not respond or progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen, only if the conditions in the managed access agreement for obinutuzumab are followed.

## 2 The technology

<b>Description of the technology</b>	Obinutuzumab (Gazyvaro, Roche Products) is a type 2 glyco-engineered antibody that binds to the CD20 protein present on B cells, except stem or plasma cells, and causes cell death.
<b>Marketing authorisation</b>	Obinutuzumab has a marketing authorisation in the UK in combination with bendamustine, followed by obinutuzumab maintenance, for the treatment of patients with follicular lymphoma 'who did not respond or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen'.
<b>Adverse reactions</b>	Common adverse reactions are upper respiratory tract infection, sinusitis, urinary tract infection, nasopharyngitis, oral herpes, rhinitis, pharyngitis, lung infection and influenza. For full details of adverse reactions and contraindications, see the summary of product characteristics.
<b>Recommended dose and schedule</b>	Obinutuzumab is given by intravenous infusion. Induction: <ul style="list-style-type: none"> <li>• Cycle 1: 1,000 mg on Day 1, Day 8 and Day 15 of the first 28-day treatment cycle</li> <li>• Cycles 2–6: 1,000 mg on Day 1 of each 28-day treatment cycle.</li> </ul> Maintenance: <ul style="list-style-type: none"> <li>• 1,000 mg every 2 months for 2 years or until disease progression (whichever occurs first).</li> </ul>
<b>Price</b>	£3,312 per 1,000-mg vial (excluding VAT; British national formulary [BNF] edition 71). The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of obinutuzumab, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The commercial arrangements included in the managed access agreement will be operationalised as a patient access scheme, agreed with the Department of Health.

## 3 Evidence

The appraisal committee (section 7) considered evidence submitted by Roche Products and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

## 4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of obinutuzumab in combination with bendamustine, having considered evidence on the nature of rituximab-refractory follicular lymphoma and the value placed on the benefits of obinutuzumab plus bendamustine by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

### ***Clinical effectiveness***

- 4.1 The committee discussed the clinical-effectiveness evidence presented by the company, its critique by the evidence review group (ERG) and evidence submitted by patient and professional groups. The clinical-effectiveness evidence for obinutuzumab in combination with bendamustine is in the company's submission (pages 52 to 108) and in the ERG's report (pages 37 to 41). In response to consultation, the company submitted additional clinical effectiveness evidence. See the [committee papers](#) for full details of the evidence, which is summarised in the slides presented at the appraisal committee meeting.

### **Clinical management of follicular lymphoma**

- 4.2 The committee discussed the current management of rituximab-refractory follicular lymphoma in the NHS and considered the potential place in the clinical-care pathway for induction with obinutuzumab plus bendamustine followed by maintenance treatment with obinutuzumab alone (O-Benda+O).
- 4.3 The committee heard that the aim of treatment for follicular lymphoma is to induce response and control disease progression for as long as possible. The clinical experts advised that many patients initially have asymptomatic slowly-progressing disease and will be on a 'watch and wait' policy until treatment becomes necessary. Once the condition has

progressed to the extent that patients need treatment, most have first-line induction with rituximab in combination with chemotherapy (R-chemotherapy) that induces a response in most people. This is followed by rituximab maintenance therapy. Rituximab monotherapy is not often used as a standard first-line treatment in clinical practice in the NHS. However the committee heard that this may change following the recent publication of NICE's guidance on non-Hodgkin's lymphoma, which recommends rituximab monotherapy as an option for stage III or IV disease which is still asymptomatic.

- 4.4 Second-line treatment for follicular lymphoma depends on the timing of relapse following first-line treatment and the chemotherapy agents used first-line. People with follicular lymphoma that does not respond to induction treatment with R-chemotherapy are considered to have uncontrolled disease, and the worst prognosis. These people are considered to have disease that is the most refractory to rituximab, and in clinical practice they may be offered bendamustine monotherapy. The clinical experts stated that patients whose disease initially responds to R-chemotherapy but relapses during, or within 6 months after, maintenance treatment are a diverse group of patients, ranging from those whose disease relapses shortly after the initiation of maintenance treatment to those who relapse following the end of 2 years of maintenance. There is variation in clinical practice but, in general, disease that relapses early-on in the 2-year rituximab maintenance period is not considered suitable for further R-chemotherapy and may be considered for treatment with bendamustine monotherapy. However disease that remains under control for some time on rituximab maintenance, or after it has stopped, is not considered to be rituximab-refractory and is likely to be treated with further R-chemotherapy (in combination with another chemotherapy agent) in preference to bendamustine monotherapy. The committee concluded that there is an unmet clinical need in patients whose disease does not respond to standard induction treatment with

R-chemotherapy, and also for patients with disease that relapses early-on in the rituximab maintenance phase.

- 4.5 The patient expert stated that follicular lymphoma is a devastating disease, which is incurable. Patients are aware that they will develop rituximab-refractory disease at some stage, after which the treatment options are limited. The patient expert stressed the importance of effective and well tolerated alternative treatments, such as bendamustine, which can also be used as an interim treatment in patients eligible for stem cell transplant. It is important for the mental wellbeing of patients to know that new treatment options are available should their disease relapse. The committee recognised that the management of follicular lymphoma is changing with the emergence of new therapeutic options. The committee concluded that new treatments for follicular lymphoma that is refractory to induction treatment with R-chemotherapy, or relapses soon after, would be welcomed by clinicians and patients.
- 4.6 The committee noted that the intention to treat population in the GADOLIN trial were people with indolent non-Hodgkin's Lymphoma. It also noted that approximately 81% had follicular lymphoma which was the population defined in the marketing authorisation of obinutuzumab. The committee was aware that patients were included in the trial if their disease was refractory to induction treatment with rituximab monotherapy, refractory to induction treatment with R-chemotherapy, or relapsed during or within 6 months of completing 2-year maintenance treatment with rituximab monotherapy. It noted that GADOLIN compared induction using obinutuzumab plus bendamustine followed by maintenance treatment with obinutuzumab alone (O-Benda+O), against induction with bendamustine alone with no maintenance therapy. The clinical experts stated that results from people in the trial who had rituximab monotherapy as induction treatment are not representative of clinical practice in England, because this is not currently standard care. They considered that the most likely use of O-Benda+O in England would be for people with disease that is

refractory to induction with R-chemotherapy, or who relapse early-on during rituximab maintenance treatment. The committee discussed the relevant comparators for O-Benda+O in clinical practice. It heard from the clinical experts that bendamustine is becoming a popular choice of first-line treatment with clinicians and patients because of its good rate of response and satisfactory tolerability. The committee also heard that if patients have bendamustine first line they would not be offered it as a second-line treatment because of cumulative toxicity. The committee concluded that people with disease that is refractory to induction with R-chemotherapy, or who relapse early-on during rituximab maintenance, are the most relevant patient group in clinical practice in the UK, and that the comparator in this group would be bendamustine.

## **Results of GADOLIN**

- 4.7 The primary outcome measure in GADOLIN was progression-free survival. The committee noted that in the intention-to-treat population there was a statistically significant improvement in median progression-free survival of 15.4 months for O-Benda+O (hazard ratio 0.47,  $p < 0.0001$ ) based on analysis of the data available in May 2015. The clinical experts considered that the median progression-free survival of 29.2 months seen in the O-Benda+O arm is considerably better than generally observed in clinical practice for patients with rituximab-refractory follicular lymphoma. The committee noted that the Kaplan–Meier curves for progression-free survival begin to diverge after 6 months, which corresponds with the end of induction treatment. The committee was uncertain whether the observed improvement in progression-free survival was due to induction treatment with obinutuzumab plus bendamustine, or to the additional obinutuzumab maintenance therapy (noting that there was no maintenance therapy in the bendamustine arm). The committee also noted that there was no difference in response rates at the end of the induction period in the two arms, which could indicate that all the benefit came from the subsequent obinutuzumab maintenance treatment. The committee heard that although there was an equivalent rate of response

in the two arms, there was some evidence of a better response in the combination arm, as shown by the data on minimum residual disease, although this is not a prognostic indicator used in routine clinical practice. The committee concluded that O-Benda+O results in longer progression-free survival than bendamustine induction treatment alone, but the mechanism and reason for this improvement is uncertain.

- 4.8 The committee noted that the overall survival data presented by the company were immature. It noted that at the May 2015 data cut, 28.1% and 18.3% of patients had died in the bendamustine-alone arm and the O-Benda+O arm respectively. The committee considered whether the statistically significant progression-free survival benefit of O-Benda+O is likely to translate into improved overall survival in the longer term. The committee discussed the potential relationship between progression-free and overall survival, but given the immaturity of the survival data it concluded that the relationship is unclear.
- 4.9 During consultation the company presented updated overall survival and progression-free survival data from GADOLIN (April 2016 data cut) as academic in confidence. The committee observed that this updated analysis was generally consistent with the analysis done in May 2015. The committee concluded that all of the data are relevant for decision making and that, although O-Benda+O is clinically effective compared to bendamustine alone for progression-free survival in follicular lymphoma, the magnitude of any overall survival gain remains uncertain.
- 4.10 The committee considered the adverse events associated with O-Benda+O. It noted that the company reported adverse-event data for all patients who had any component of obinutuzumab or bendamustine treatment in GADOLIN, and 98.8% of patients in both trial arms had at least 1 adverse event. In the O-Benda+O arm 39.0% of patients had a serious adverse event compared with 34.5% in the bendamustine monotherapy arm. The committee concluded that the safety profile of O-Benda+O is similar to that of bendamustine alone.

### ***Cost effectiveness***

- 4.11 The committee discussed the cost-effectiveness evidence presented by the company and its critique by the ERG. The cost-effectiveness evidence is in the company's submission (pages 109 to 176), in the company's response to clarification and in the ERG's report (pages 78 to 140). In response to consultation, the company submitted additional cost-effectiveness analyses based on an updated patient access scheme and incorporating the latest update of the clinical evidence.
- 4.12 The company originally submitted a de novo model health state transition Markov model which compared O-Benda+O with bendamustine alone in patients with rituximab-refractory follicular lymphoma. During consultation the company submitted an updated model based on a partitioned-survival modelling approach. This model included all of the key amendments recommended by the ERG on the model in the original submission. The committee noted that similar models had been used in other follicular lymphoma appraisals. The committee noted that the model population was based on GADOLIN (updated April 2016 data) and combined patients with follicular lymphoma that was refractory to induction treatment with rituximab monotherapy or R-chemotherapy, or was refractory during, or within 6 months of completing maintenance treatment with rituximab monotherapy. It discussed whether it was more appropriate to consider particular subgroups of patients or the model population as a whole. It acknowledged that it had previously heard that clinicians would consider O-Benda+O to be potentially most useful in patients whose disease was refractory to R-chemotherapy induction (see section 4.4), and that the ERG had done an exploratory analysis in this patient population. However it agreed that the population who might be offered this combination in clinical practice was potentially broader than just people with R-chemotherapy refractory disease, and that the subgroups were small, adding additional uncertainty to the immature overall survival data. The committee therefore concluded that the



structure of the company's model was acceptable and that it would not limit its consideration to a subgroup with R-chemotherapy refractory disease.

- 4.13 The company base case, updated post-consultation assumed that the treatment effect of O–Benda+O would last 5.5 years (overall survival up to the last observed event at 4 years, and then overall survival data extrapolated for a further 18 months because of no additional deaths). The base case ICER was higher than is normally considered to be a cost effective use of NHS resources. The committee considered the company's scenario analyses, which showed that the ICER was particularly sensitive to the duration of the expected treatment effect of O–Benda+O on overall survival. In light of the immature survival data the company also supplied a cost-effectiveness analysis using a treatment effect on overall survival of 7 years, which lowered the ICER. The committee acknowledged that the ERG's exploratory analysis of the company's revised model resulted in cost-effectiveness estimates that were similar to the company's. The committee noted that the ERG's ICER for O–Benda+O was only below the range that is normally considered cost effective when treatment effect on overall survival of 25 years was assumed. If a more conservative 4-year treatment effect was assumed, both the company's and the ERG's ICERs were well above this range. The committee therefore concluded that O–Benda+O is not a cost-effective use of NHS resources but that it may become cost effective if the treatment effect on survival persists for between 7 and 25 years. The committee considered other areas of uncertainty in the cost-effectiveness modelling. It noted that because the cost-effectiveness estimates are largely dependent on the duration of the treatment effect on overall survival, the cost effectiveness estimates should be based on the final analysis of the GADOLIN trial (which reports in 2019). The committee was aware that the progression-free survival results are promising, and were reminded by the patient expert of the value to patients of progression-free survival. However, the company's

and the ERG's base case cost-effectiveness estimates are above the level that could be accepted as a cost-effective use of NHS resources.

### ***Cancer Drugs Fund***

4.14 Having concluded that O–Benda+O could not be recommended for routine use, the committee then considered if it could be recommended for treating rituximab-refractory follicular lymphoma within the Cancer Drugs Fund. The committee discussed the new arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the addendum to the NICE process and methods guides. Under the new arrangements, drugs that appear promising, but for which the evidence is not robust enough for routine use, may be given a conditional recommendation by NICE and made available to NHS patients through the Cancer Drugs Fund. The committee was aware that in considering this, the following criteria must be met:

- the ICERs have the plausible potential for satisfying the criteria for routine use
- it is possible that the clinical uncertainty can be addressed through collection of outcome data from patients treated in the NHS
- it is possible that the data will be able to inform a subsequent update of the guidance.

4.15 The committee noted that the company's base case ICER was above the range normally considered to be a cost effective use of NHS resources. The committee agreed that the company's scenario analysis exploring a different duration of treatment effect on overall survival indicated a plausible potential for O–Benda+O to be cost effective with its updated patient access scheme. This is because the committee considered that it was plausible that the treatment effect was longer than modelled in the company's base case. However, the committee noted that the company's revised cost-effectiveness estimates were based on immature overall survival data from GADOLIN, but more mature overall survival data was

likely to be available by December 2020. The committee considered that the availability of more mature overall survival data from GADOLIN was likely to resolve the uncertainty around the treatment effect and may give a more robust cost effectiveness estimate. The committee therefore considered that the ongoing research may help inform a subsequent update of the guidance. The committee also acknowledged that data collected from use in the NHS through the Cancer Drugs Fund would offer further supportive evidence on the clinical effectiveness of O–Benda+O. The committee therefore recommended O-Benda+O as an option for use within the Cancer Drugs Fund for people with follicular lymphoma that has not respond or progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen if the conditions in the managed access agreement for obinutuzumab are followed.

**Summary of appraisal committee’s key conclusions**

TAXXX	Appraisal title: Obinutuzumab with bendamustine for treating follicular lymphoma refractory to rituximab	Section
<b>Key conclusion</b>		
Obinutuzumab in combination with bendamustine followed by obinutuzumab maintenance is recommended for use within the Cancer Drugs Fund for treating adults with follicular lymphoma that did not respond or progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen if the conditions in the managed access agreement for obinutuzumab are followed.		1.1
During consultation the company presented updated overall survival and progression-free survival data from GADOLIN (April 2016 data cut) as academic in confidence. The committee observed that this updated analysis was generally consistent with the analysis done in		4.9

<p>May 2015. The committee concluded that all of the data are relevant for decision making and that, although O-Benda+O is clinically effective compared to bendamustine alone for progression-free survival in follicular lymphoma, the magnitude of any overall survival gain remains uncertain.</p> <p>The committee was reassured that the ERG’s exploratory analysis of the company’s revised model resulted in cost-effectiveness estimates that were similar to the company’s but noted that the ERG’s incremental cost-effectiveness ratio (ICER) for O–Benda+O was only within the range which would normally be considered cost effective when the treatment effect was between 7 and 25 years . If a more conservative 4 year treatment effect was assumed, both the company’s and the ERG’s ICERs were well above this range. The committee therefore concluded that O–Benda+O is not a cost-effective use of NHS resources.</p>	4.13	
<b>Current practice</b>		
<p>Clinical need of patients, including the availability of alternative treatments</p>	<p>The committee understood that follicular lymphoma is a devastating disease, which is incurable. Patients are aware that they will develop rituximab-refractory disease at some stage, after which the treatment options are limited. The committee heard about the importance of effective and well tolerated alternative treatments, such as bendamustine, which can also be used as an interim treatment in patients eligible for stem cell transplant. It is important for the mental wellbeing of patients to know that new treatment options are available should their disease relapse. The committee recognised</p>	4.5

	<p>that the management of follicular lymphoma is changing with the emergence of new therapeutic options. The committee concluded that new treatments for follicular lymphoma that is refractory to induction treatment with R-chemotherapy would be welcomed by clinicians and patients.</p>	
<p><b>The technology</b></p>		
<p>Proposed benefits of the technology</p> <p>How innovative is the technology in its potential to make a significant and substantial impact on health-related benefits?</p>	<p>The committee did not identify any specific health related benefit that had not already been captured in the quality-adjusted life year (QALY) calculation.</p>	<p>–</p>
<p>What is the position of the treatment in the pathway of care for the condition?</p>	<p>The committee heard that in clinical practice, people with disease that is refractory to induction with rituximab in combination with chemotherapy (R-chemotherapy), or who relapse early-on during rituximab maintenance treatment, are considered for treatment with bendamustine. The committee also considered patients whose disease initially responds to R-chemotherapy, but relapses during or within 6 months after maintenance treatment. The clinical experts said that there is variation in clinical practice but, in general, people whose disease relapses early-on in the</p>	<p>4.4</p>

	<p>2-year rituximab maintenance period are not considered suitable for further R-chemotherapy and may be considered for bendamustine monotherapy.</p> <p>The committee concluded that O-Benda+O is most likely to be used in patients whose disease does not respond to standard induction treatment with R-chemotherapy, and also for patients who become refractory early-on in the rituximab maintenance phase.</p>	
Adverse reactions	<p>The committee considered the adverse events associated with O-Benda+O. It noted that the company reported adverse-event data for all patients who had any component of obinutuzumab or bendamustine treatment in the GADOLIN trial. The committee concluded that the safety profile of O-Benda+O is similar to that of bendamustine alone.</p>	4.10
<b>Evidence for clinical effectiveness</b>		
Availability, nature and quality of evidence	<p>The committee noted that intention to treat population in the GADOLIN trial were people with indolent non-Hodgkin's Lymphoma. It also noted that approximately 81% had follicular lymphoma which was the population defined in the marketing authorisation of obinutuzumab. The committee was aware that patients were included in the trial if their disease was refractory to induction treatment with rituximab monotherapy, refractory to induction treatment with R-chemotherapy, or</p>	4.6

	relapsed during or within 6 months of completing 2-year maintenance treatment with rituximab monotherapy. It noted that GADOLIN compared induction using obinutuzumab plus bendamustine followed by maintenance treatment with obinutuzumab alone (O-Benda+O), against induction with bendamustine alone with no maintenance therapy.	
Relevance to general clinical practice in the NHS	The committee concluded that people with disease that is refractory to induction with R-chemotherapy, or who relapse early-on during rituximab maintenance, are the most relevant patient group in clinical practice in the UK, and that the comparator in this group would be bendamustine.	4.6
Uncertainties generated by the evidence	During consultation the company presented updated overall survival and progression-free survival data from GADOLIN (April 2016 data cut) as academic in confidence. The committee observed that this updated analysis was generally consistent with the analysis done in May 2015. The committee concluded that all of the data are relevant for decision making and that, although O-Benda+O is clinically effective compared to bendamustine alone for progression-free survival in follicular lymphoma, the magnitude of any overall survival gain remains uncertain.	4.9

<p>Are there any clinically relevant subgroups for which there is evidence of differential effectiveness?</p>	<p>The committee considered people with follicular lymphoma that did not respond to induction treatment with R-chemotherapy or early-on in rituximab maintenance therapy to be most relevant. The differential effectiveness in this combined subgroup was not considered.</p>	<p>—</p>
<p>Estimate of the size of the clinical effectiveness including strength of supporting evidence</p>	<p>The primary outcome measure in GADOLIN was progression-free survival. The committee noted that in the intention-to-treat population there was a statistically significant improvement in median progression-free survival of 15.4 months for O-Benda+O (hazard ratio 0.47, <math>p &lt; 0.0001</math>).</p>	<p>4.7</p>
<p><b>Evidence for cost effectiveness</b></p>		
<p>Availability and nature of evidence</p>	<p>The committee discussed the cost-effectiveness evidence presented by the company and its critique by the ERG. The cost-effectiveness evidence is in the company's submission (pages 109 to 176), in the company's response to clarification and in the ERG's report (pages 78 to 140). In response to consultation, the company submitted additional cost-effectiveness analyses based on an updated patient access scheme and incorporating the latest update of the clinical evidence.</p>	<p>4.11 4.12</p>



	<p>The company originally submitted a de novo model health state transition Markov model which compared O Benda+O with bendamustine alone in patients with rituximab-refractory follicular lymphoma. During consultation the company submitted an updated model based on a partitioned-survival modelling approach. This model included all of the key amendments recommended by the ERG on the model in the original submission. During consultation the company submitted revised cost-effectiveness estimates, based on the updated results from GADOLIN and a revised patient access scheme.</p> <p>The committee concluded that the structure of the company’s model was acceptable. The committee was aware that the subgroup of particular interest in the trial was people with follicular melanoma refractory to R-chemotherapy. However it agreed that the population who might be offered this combination in clinical practice was potentially broader than just people with R-chemotherapy refractory disease.</p>	
<p>Uncertainties around and plausibility of assumptions and inputs in the economic model</p>	<p>The committee considered the company’s scenario analyses, which showed that the ICER was particularly sensitive to the duration of the expected treatment benefit for O-Benda+O. The company’s revised base-case analysis was based on an estimated</p>	<p>4.13</p>

	<p>treatment effect of 5.5 years (overall survival up to the last observed event at 4 years, and then overall survival data extrapolated for a further 18 months because of no additional deaths). The company also supplied a cost-effectiveness analysis using a treatment effect of 7 years, which lowered the ICER.</p>	
<p>Incorporation of health-related quality-of-life benefits and utility values</p> <p>Have any potential significant and substantial health-related benefits been identified that were not included in the economic model, and how have they been considered?</p>	<p>The committee was aware of the utility values in the company's model and considered the impact on the ICER of using the ERG's alternative estimates.</p> <p>None identified.</p>	4.14
<p>Are there specific groups of people for whom the technology is particularly cost effective?</p>	<p>No groups were identified.</p>	–

<p>What are the key drivers of cost effectiveness?</p>	<p>The committee noted that the cost-effectiveness estimates were largely dependent on the duration of the treatment effect on overall survival. It noted that that the ERG's ICER for O-Benda+O was within the range which would normally be considered cost effective when the treatment effect was between 7 and 25 years. If a more conservative 4-year treatment effect was assumed, both the company's and the ERG's ICERs were well above this range.</p>	<p>4.13</p>
<p>Most likely cost-effectiveness estimate (given as an ICER)</p>	<p>The committee noted that the company's and the ERG's base-case cost-effectiveness estimates (which are commercial in confidence and cannot be shown) were above the level that could be accepted as a cost-effective use of NHS resources.</p>	<p>4.13</p>
<p><b>Additional factors taken into account</b></p>		
<p>Patient access schemes (PPRS)</p>	<p>The pricing arrangement considered during guidance development was that the company had agreed a patient access scheme with the Department of Health. This scheme would provide a simple discount to the list price of obinutuzumab with the discount applied at the point of purchase or invoice. The commercial arrangements included in the managed access agreement will be operationalised as a patient access scheme, registered with the Department of Health.</p>	

End-of-life considerations	Not applicable.	—
Cancer Drugs Fund	The committee considered that the availability of more mature overall survival data from GADOLIN may resolve the uncertainty around the treatment effect and that the ICER for O Benda+O compared with bendamustine alone may fall within the range considered to be cost effective. The committee therefore considered that the ongoing research may help inform a subsequent update of the guidance. The committee concluded that O Benda+O met the criteria to be recommended in the Cancer Drugs Fund as an option for people with follicular lymphoma that did not respond or progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen if the company provides it with the discount agreed in the patient access scheme and conditions in the managed access agreement for obinutuzumab are followed. .	4.15
Equalities considerations and social value judgements	No equalities issues were identified.	—

## 5 Implementation

- 5.1 When NICE recommends a treatment as an option for use within the Cancer Drugs Fund, NHS England will make it available within the conditions of the managed access agreement. This means that, if a patient has follicular that did not respond or progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen and the doctor responsible for their care thinks that obinutuzumab is the right treatment, it should be available for use, in line with NICE's recommendations and the Cancer Drugs Fund criteria in the managed access agreement. Further information can be found in [NHS England's Appraisal and Funding of Cancer Drugs from July 2016 \(including the new Cancer Drugs Fund\) - A new deal for patients, taxpayers and industry](#)
- 5.2 NHS England and Roche have a managed access agreement that makes obinutuzumab available to the NHS at a reduced cost. The commercial arrangements included in the managed access agreement will be operationalised as a patient access scheme, registered with the Department of Health. The Department of Health and Roche have agreed that obinutuzumab will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to **[NICE to add details at time of publication]**

## 6 Recommendations for data collection

- 6.1 As a condition of the positive recommendation and the managed access agreement, the company is required to collect updated efficacy data from the GADOLIN study.

## 7 Review of guidance

- 7.1 This guidance will be updated when the data collection period is concluded. This is anticipated to be December 2020, when the final analysis of the GADOLIN study is expected to be available. The process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start.
- 7.2 As part of the managed access agreement, the technology will continue to be available via the Cancer Drugs Fund after the data collection period has ended and while the guidance is being updated. This assumes that the data collection period ends as planned and the review of guidance follows the standard timelines described in the [addendum](#) to NICE's methods and processes when appraising cancer technologies.

Jane Adam  
Chair, appraisal committee  
July 2017

## 8 Appraisal committee members and NICE project team

### ***Appraisal committee members***

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee A](#).

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The [minutes](#) of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

***NICE project team***

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

**Helen Tucker**

Technical Lead

**Eleanor Donegan**

Technical Adviser

**Liv Gualda, Leanne Wakefield and Marcia Miller**

Project Manager

ISBN: [to be added at publication]