NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia (TA663)

Published: December 2020

Summary

NICE has recommended venetoclax with obinutuzumab as an option for treating adults with untreated chronic lymphocytic leukaemia (see section 1.1 for further details).

We estimate that:

- 1,479 people with chronic lymphocytic leukaemia (CLL) are eligible for treatment with venetoclax plus obinutuzumab each year. This is 187 people with CLL and a 17p deletion or TP53 mutation and 1,292 people with CLL and no 17p deletion or TP53 mutation.
- 1,210 people will have venetoclax plus obinutuzumab as a first-line treatment from 2022/23 onwards once uptake has reached 82% as shown in table 1.

Table 1 Estimated number of people in England having venetoclax with obinutuzumab

	2021/22	2022/23	2023/24	2024/25	2025/26
Uptake rate for venetoclax with obinutuzumab (%)	41%	82%	82%	82%	82%
Population having venetoclax with obinutuzumab each year	605	1,210	1,210	1,210	1,210

This report is supported by a local resource impact template because the list price of venetoclax with obinutuzumab has a discount that is commercial in confidence. The discounted price of venetoclax with obinutuzumab can be put into the template and other variables may be amended.

There is an anticipated reduction in patients receiving a second line treatment as a result of venetoclax with obinutuzumab being used as a first-line treatment as shown in table 2.

Table 2 Estimated number of people starting each second-line treatment after the implementation of venetoclax plus obinutuzumab (as a first-line treatment) using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
Population having venetoclax monotherapy each year	88	84	73	66	66
Population having venetoclax plus rituximab each year	244	231	164	109	109
Population having ibrutinib each year	244	236	181	135	135
Total	**575**	**550**	**418**	**309**	**309**

Within this technology appraisal (TA663) venetoclax plus obinutuzumab is also recommended for use within the Cancer Drugs Fund (CDF) as an option for untreated CLL in adults with no 17p deletion or TP53 mutation, for whom fludarabine plus cyclophosphamide and rituximab, or bendamustine plus rituximab is suitable (see section 1.2 for further details). This has not been included in the resource impact template as the cost of this does not affect routine commissioning.

This technology is commissioned by NHS England. Providers are NHS hospital trusts.

1 Venetoclax plus obinutuzumab

1.1 NICE has recommended venetoclax plus obinutuzumab as an option for untreated chronic lymphocytic leukaemia (CLL) in adults 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.

1.2 Venetoclax plus obinutuzumab is recommended for use within the Cancer Drugs Fund (CDF) 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.

1.3 People with untreated CLL are offered different treatments depending on whether they are likely to tolerate chemo-immunotherapy, and whether they have certain genetic abnormalities (such as a 17p deletion or TP53 mutation). In people with a 17p deletion or TP53 mutation, CLL does not usually respond well to standard chemo-immunotherapy, and ibrutinib is usually used.

In people without a 17p deletion or TP53 mutation, FCR or BR are the most common chemo-immunotherapies used. If FCR or BR is unsuitable, obinutuzumab plus chlorambucil is used.

1.4 Clinical trial evidence shows that, in people without a 17p deletion or TP53 mutation for whom FCR or BR is unsuitable, CLL treated

with venetoclax plus obinutuzumab takes longer to progress than CLL treated with obinutuzumab plus chlorambucil.

2 Resource impact of the guidance

2.1 We estimate that:

- 1,479 people with CLL are eligible for treatment with venetoclax with obinutuzumab each year. This is 187 people with a 17p deletion or TP53 mutation and 1,292 with no 17p deletion or TP53 mutation.
- 1,210 people will have venetoclax with obinutuzumab from year 2 onwards once uptake has reached 82% as shown in table 1. This is 47 people with a 17p deletion or TP53 mutation (which is 25% of the eligible population) and 1,163 people with no 17p deletion or TP53 mutation (which is 90% of the eligible population).

2.2 The current treatment and future uptake figure assumptions are based on clinical expert opinion and are shown in the resource impact template. Table 3 shows the number of people in England who are estimated to have venetoclax plus obinutuzumab as first-line treatment by financial year and Table 4 shows the number of people having a second-line treatment after the implementation of venetoclax plus obinutuzumab as a first-line treatment.

Table 3 Estimated number of people having first-line treatment with venetoclax plus obinutuzumab using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
Uptake rate for venetoclax plus obinutuzumab (%)	41%	82%	82%	82%	82%
Population having venetoclax plus obinutuzumab each year	605	1,210	1,210	1,210	1,210

Table 4 Estimated number of people starting each second-line treatment after the implementation of venetoclax plus obinutuzumab (as a first-line treatment) using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
Population having venetoclax monotherapy each year	88	84	73	66	66
Population having venetoclax plus rituximab each year	244	231	164	109	109
Population having ibrutinib each year	244	236	181	135	135
Total	**575**	**550**	**418**	**309**	**309**

2.3 This report is supported by a local resource impact template. There are commercial arrangements in place for venetoclax and obinutuzumab (simple discount patient access schemes) which make them available to the NHS with discount. The discounted price of venetoclax plus obinutuzumab can be put into the template and other variables may be amended. It is the company's responsibility to let relevant NHS organisations know details of the discount.

2.4 The resource impact of venetoclax monotherapy (TA487) as a second-line treatment is covered by the Cancer Drugs Fund budget.

3 Implications for commissioners

3.1 This technology is commissioned by NHS England. Providers are NHS hospital trusts.

3.2 Recommendation 1.1 will have a resource impact on routine commissioning. This is discussed in section 2.

3.3 Recommendation 1.2 will not have a resource impact on routine commissioning because of its inclusion in the Cancer Drugs Fund. The resource impact will be covered by the Cancer Drugs Fund.

3.4 The use of venetoclax monotherapy as a second-line treatment (TA487) is part of the Cancer Drugs Fund so will not have a resource impact on routine commissioning.

3.5 Venetoclax plus obinutuzumab falls within the programme budgeting category 02I, Cancer and Tumours, Cancer, Haematological.

4 How we estimated the resource impact

The population

4.1 Around 3,200 people were diagnosed with CLL in 2017 (Cancer registration statistics for England, 2017). Table 5 shows the details of the population with CLL who are estimated to be eligible for treatment with venetoclax plus obinutuzumab.

Table 5 Number of people eligible for treatment in England

Population	Proportion of previous row (%)	Number of people
Total population		54,786,327
Adult population		44,022,560
Incidence of CLL[1]	0.01	3,157
Untreated people with CLL that are expected to have treatment[2]	67	2,115
Number of people with a 17p deletion or TP53 mutation[3]	9	187
Number of people eligible for treatment with venetoclax plus obinutuzumab[3]	100	187
Number of people estimated to have venetoclax plus obinutuzumab each year from year 2[4]	25	47
Number of people with no 17p deletion or TP53 mutation[3]	91 (of 2,115)	1,929
Number of people unsuitable for FCR or BR[5]	67	1,292
Number of people eligible for treatment with venetoclax plus obinutuzumab[4]	100	1,292
Number of people estimated to have venetoclax plus obinutuzumab each year from year 2[4]	90	1,163
Total number of people estimated to have venetoclax plus obinutuzumab each year from year 2		1,210

[1] Cancer registration statistics for England, 2017, ICD 10 code C91.1
[2] Company submission
[3] Company submission/NHSE
[4] Clinical expert opinion
[5] CLL disease registry

Assumptions

4.2 The resource impact template assumes that:

- all people with a 17p deletion or TP53 mutation are currently treated with ibrutinib as a first-line treatment
  - in year 1 12.5% of this group of people will be treated with venetoclax plus obinutuzumab and 87.5% with ibrutinib

  - from year 2 onwards 25% of this group of people will be treated with venetoclax plus obinutuzumab and 75% with ibrutinib
- all people with no 17p deletion or TP53 mutation are currently treated with obinutuzumab plus chlorambucil as a first-line treatment
  - in year 1 45% of this group will be treated with venetoclax plus obinutuzumab and 55% with obinutuzumab plus chlorambucil
  - from year 2 onwards 90% of this group of people will be treated with venetoclax plus obinutuzumab and 10% with obinutuzumab plus chlorambucil

- the dose of venetoclax plus obinutuzumab is:

<u>Venetoclax</u>

  - 20 mg of venetoclax daily on days 22 to 28 of the first cycle followed by
  - 50 mg daily on days 1 to 7, 100 mg daily on days 8 to 14, 200 mg daily on days 15 to 21 and 400 mg daily on days 22 to 28 of the second cycle
  - cycles 3 to 12 consist of 400 mg daily
  - each cycle is 28 days long and it is assumed that there are 12 cycles. The medication is taken orally at home.

<u>Obinutuzumab</u>

  - the initial dose of obinutuzumab is 3 infusions each of 1,000 mg followed by 1,000 mg on day 1 of cycles 2 to 6
  - there are 6 cycles in total and the drug is administrated intravenously
- the relevant tariff for the first 6 cycles of treatment when both drugs are administered is SB12Z Deliver Simple Parenteral Chemotherapy at First Attendance which has a tariff of £159. (National tariff 20/21)

- the first cycle with the additional 2 intravenous administrations of obinutuzumab is SB13Z Deliver more complex parenteral chemotherapy at first Attendance and SB15Z Deliver Subsequent Elements of a Chemotherapy Cycle which both have a tariff of £319 per attendance(National tariff 20/21).
- the last 6 cycles of treatment which is the administration of only venetoclax is SB11Z Deliver Exclusively Oral Chemotherapy which has a tariff of £127 per attendance (National tariff 20/21).

- the dosages and cycles of obinutuzumab are the same when administered with chlorambucil as when administered with venetoclax
- the dose of chlorambucil is 0.5 mg per kg on days 1 and 15 of each cycle, for 12 cycles. It is an oral medication taken at home.
- the relevant tariff for the first 6 cycles of treatment when both drugs are administered is SB12Z Deliver Simple Parenteral Chemotherapy at First Attendance which has a tariff of £159 (National tariff 20/21)
- the first cycle with the additional 2 intravenous administrations of obinutuzumab is SB13Z Deliver more complex parenteral chemotherapy at first Attendance and SB15Z Deliver Subsequent Elements of a Chemotherapy Cycle which both have a tariff of £319 per attendance(National tariff 20/21)
- the last 6 cycles of treatment, administrating only chlorambucil is SB11Z Deliver Exclusively Oral Chemotherapy which has a tariff of £127 per attendance (National tariff 20/21)

- ibrutinib is taken daily at a dose of three 140 mg tablets, totaling 420 mg. The average treatment duration is 32 months based on TA429.
- every month the drug is administered is SB11Z Deliver Exclusively Oral Chemotherapy which has a tariff of £128 per attendance (National tariff 20/21).

- in people with a 17p deletion or TP53 mutation who receive first-line treatment of venetoclax plus obinutuzumab, 20% will receive second-line treatment in year 2 and 36.2% of people will receive it in year 3. It is assumed that all these people will have ibrutinib as the second-line treatment
- 16.3% of people with a 17p deletion or TP53 mutation will receive second-line treatment with venetoclax monotherapy in year 2 and 30.5% will receive it in year 3.
- 4.6% of people with no 17p deletion or TP53 mutation who receive first-line treatment with venetoclax plus obinutuzumab will receive second-line treatment in year 2 and 9.9% of them will receive it in year 3. It is assumed that half of these people have ibrutinib as second-line treatment and the remaining half will have venetoclax plus rituximab.
- 8.9% of people with no 17p deletion or TP53 mutation who receive first-line treatment with venetoclax plus chlorambucil will receive second-line treatment in year 2 and 28.8% of them will receive it in year 3. It is assumed that half of these people will receive ibrutinib and half will have venetoclax plus rituximab as second-line treatment.

- in second-line treatment ibrutinib is taken daily in tablet form at a dose of three 140 mg tablets, totaling 420 mg. Average treatment duration is 44 months based on TA561.
- every month the drug is administered is SB11Z Deliver Exclusively Oral Chemotherapy which has a tariff of £127 per attendance (National tariff 20/21).

- venetoclax monotherapy is covered by the Cancer Drugs Fund and therefore is not assessed in this report, please see TA487 for further information.

- the dosages and cycles of venetoclax are the same when administered with rituximab as when administered with obinutuzumab.
- the loading dose of rituximab is:
  - 375 mg per m^2 on day 1 of cycle 1
- cycles 2-6 consist of 500 mg per m^2 on day 1 of each cycle
- each cycle is 28 days long and it is assumed that there are 6 cycles. The drug is administrated intravenously.
- the first 6 months of administration when both drugs are administered is SB12Z Deliver Simple Parenteral Chemotherapy at First Attendance which has a tariff of £159 (National tariff 20/21).
- all remaining months when venetoclax is administered is under SB11Z Deliver Exclusively Oral Chemotherapy which has a tariff of £127 (National tariff 20/21).

Other factors

4.3 With home-based oral treatments there may be a decreased need for hospital capacity in order to administer the treatments compared with the current treatments being hospital-based intravenous infusions.

4.4 The use of venetoclax plus obinutuzumab could decrease the carbon footprint arising from hospital-based intravenous infusions as a result of people switching treatment to home-based oral tablets.

About this resource impact report

This resource impact report accompanies the NICE guidance on Venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia and should be read with it.