NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Acalabrutinib for treating chronic lymphocytic leukaemia (TA689)

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Summary

NICE has recommended acalabrutinib as monotherapy as an option for treating adults with chronic lymphocytic leukaemia (CLL) in adults (see section 1.1 for further details).

This report and the associated resource impact template cover both the impact of this technology appraisal (for acalabrutinib) and TA663 venetoclax with obinutuzumab . They both look at the impact on people with CLL in the first-line and second-line of treatment who are ineligible for fludarabine plus cyclophosphamide and rituximab (FCR), or bendamustine plus rituximab (BR).

This report and template also cover one additional population to the population covered by TA663. This is people with no 17p deletion or TP53 mutation who were previously treated with (FCR) or (BR).

We estimate that:

- 1,479 people with untreated CLL are eligible for treatment with acalabrutinib monotherapy each year. This is 187 people with untreated CLL and a 17p deletion or TP53 mutation and 1,292 people with untreated CLL and no 17p deletion or TP53 mutation.
- 1,201 people will start acalabrutinib monotherapy as a first-line treatment from 2025/26 onwards once uptake has reached 81% as shown in table 1.

Table 1 Estimated number of people in England starting acalabrutinib monotherapy using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
People eligible for and starting first-line treatment	**1,479**	**1,479**	**1,479**	**1,479**	**1,479**
Uptake rate for acalabrutinib (%)	36	72	74	81	81
Population starting acalabrutinib monotherapy each year	526	1,062	1,099	1,192	1,201

NICE has also recommended acalabrutinib monotherapy, within its marketing authorisation, as an option for previously treated CLL in adults (see section 1.2 for further details).

We estimate that:

- 757 people with previously treated CLL are expected to be eligible for a second-line treatment in year 1, decreasing to 552 in year 5. This decrease is because the percentage of people having a second-line treatment after acalabrutinib is lower than some of the other treatment options.
- The percentage of these people initiating acalabrutinib each year is shown below.

Table 2 Estimated number of people who start a second-line treatment of acalabrutinib in year using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
People eligible for and starting second-line treatment	**757**	**700**	**471**	**426**	**552**
Uptake rate for acalabrutinib (%)	42	61	68	61	46
Population starting acalabrutinib each year	320	425	318	259	255

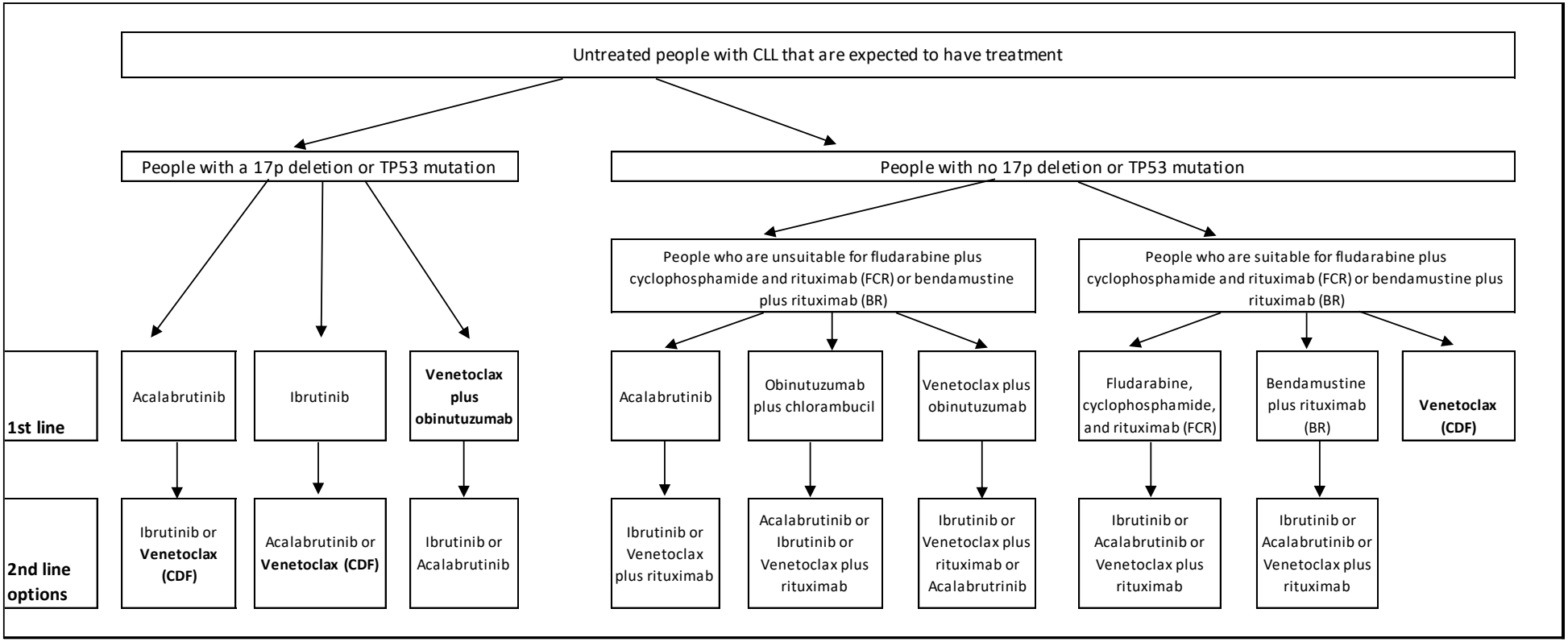
This table does not include people who continue second-line treatment beyond the initial 12 months.

To see further information on the patient pathway please see figure 1 on the next page.

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

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

Figure 1


Untreated people with CLL that are expected to have treatment
People with a 17p deletion or TP53 mutation
People with no 17p deletion or TP53 mutation
People who are unsuitable for fludarabine plus cyclophosphamide and rituximab (FCR) or bendamustine plus rituximab (BR)
People who are suitable for fludarabine plus cyclophosphamide and rituximab (FCR) or bendamustine plus rituximab (BR)
1st line
Acalabrutinib
Ibrutinib
Venetoclax plus obinutuzumab
Acalabrutinib
Obinutuzumab plus chlorambucil
Venetoclax plus obinutuzumab
Fludarabine, cyclophosphamide, and rituximab (FCR)
Bendamustine plus rituximab (BR)
Venetoclax (CDF)
2nd line options
Ibrutinib or Venetoclax (CDF)
Acalabrutinib or Venetoclax (CDF)
Ibrutinib or Acalabrutinib
Ibrutinib or Venetoclax plus rituximab
Acalabrutinib or Ibrutinib or Venetoclax plus rituximab
Ibrutinib or Venetoclax plus rituximab or Acalabrutrinib
Ibrutinib or Acalabrutinib or Venetoclax plus rituximab
Ibrutinib or Acalabrutinib or Venetoclax plus rituximab

1 Acalabrutinib monotherapy

1.1 NICE has recommended acalabrutinib monotherapy 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 drug according to the commercial arrangements.

1.2 Acalabrutinib as monotherapy is recommended, within its marketing authorisation, as an option for previously treated CLL in adults. It is recommended only if the company provides the drug according to the commercial arrangement.

1.3 NICE has also recently recommended venetoclax plus obinutuzumab as an option for untreated CLL in adults, please see TA663 for more information.

1.4 People with untreated CLL that has 17p deletion or TP53 mutation usually have ibrutinib. The company assumed that acalabrutinib is as effective as ibrutinib in a cost-minimisation analysis. Despite the uncertainties, acalabrutinib is likely to be cost saving compared with ibrutinib.

1.5 People with untreated CLL without a 17p deletion or TP53 mutation usually have FCR or BR. If FCR or BR are unsuitable, chlorambucil plus obinutuzumab is offered instead. Clinical trial evidence in this group shows that CLL takes longer to progress when treated with acalabrutinib compared with chlorambucil plus obinutuzumab.

1.6 People with previously treated CLL that has relapsed or does not respond to treatment, usually have ibrutinib or venetoclax plus

rituximab. For this group, acalabrutinib has not been directly compared with ibrutinib or with venetoclax plus rituximab. The results of an indirect comparison with ibrutinib are uncertain. The company assumed that acalabrutinib was as effective as ibrutinib in the cost-minimisation analyses. Despite the uncertainty, acalabrutinib is likely to be cost saving compared with ibrutinib.

2 Resource impact of the guidance

2.1 We estimate that:

- 1,479 people with untreated CLL are eligible for treatment with acalabrutinib each year. This is 187 people with a 17p deletion or TP53 mutation and 1,292 with no 17p deletion or TP53 mutation.
- 1,201 people will start on acalabrutinib from year 5 onwards once uptake has reached 81% as shown in table 3. This is 103 people with untreated CLL and a 17p deletion or TP53 mutation (which is 55% of the eligible population) and 1,098 people with untreated CLL and no 17p deletion or TP53 mutation (which is 85% of the eligible population).
- 757 people with previously treated CLL are expected to be eligible to start second-line treatment in year 1, decreasing to 552 in year 5. This decrease is because the percentage of people having a second-line treatment after acalabrutinib is lower than some of the other treatment options. The percentage of these people starting acalabrutinib each year is shown below in table 4.

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 acalabrutinib as first-line treatment by financial year.

Table 3 Estimated number of people starting a first-line treatment with acalabrutinib monotherapy using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
People eligible for and starting first-line treatment	**1,479**	**1,479**	**1,479**	**1,479**	**1,479**
Uptake rate for acalabrutinib (%)	36	72	74	81	81
Population starting acalabrutinib monotherapy each year	526	1,062	1,099	1,192	1,201
Uptake rate of people that will have a second-line treatment	36%	33%	22%	20%	26%
Population having second-line treatment each year	757	700	471	426	552

Table 4 Estimated number of people who start a second-line treatment of acalabrutinib in year using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
People eligible for and starting second-line treatment	**757**	**700**	**471**	**426**	**552**
Uptake rate for acalabrutinib (%)	42	61	68	61	46
Population starting acalabrutinib each year	320	425	318	259	255

This table does not include people who continue second-line treatment beyond the initial 12 months.

2.3 This report is supported by a local resource impact template. The company has a commercial arrangement (simple discount patient access scheme) which make acalabrutinib available to the NHS with discount. The discounted price of acalabrutinib 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. There are also commercial arrangements in place for the other comparator treatments.

3 Implications for commissioners

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

3.2 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.

3.3 Acalabrutinib 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 acalabrutinib monotherapy.

Table 5 Number of people eligible for first-line 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 acalabrutinib[3]	100	187
Number of people estimated to start acalabrutinib each year from year 5[3]	55	103
Number of people with no 17p deletion or TP53 mutation[3]	91 (of 2,115)	1,929
Number of people suitable for FCR or BR[4]	33	636
Number of people unsuitable for FCR or BR[4]	67(of 1,929)	1,292
Number of people eligible for treatment with acalabrutinib [3]	100	1,292
Number of people estimated to start acalabrutinib each year from year 4[3]	85	1,098
Total number of people estimated to have acalabrutinib each year from year 5	(103 + 1098)	1,201

[1] Cancer registration statistics for England, 2017, ICD 10 code C91.1

[2] Company submission

[3] Clinical expert opinion

[4] Clincial expert opinion/TA663

Table 6 Number of people eligible for second-line 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 a first-line treatment[2]	67	2,115
Number of people eligible for a second-line treatment in year 5[3]	26	552
Number of people starting acalabrutinib in year 5 as a second-line treatment[3]	46	255

[1] Cancer registration statistics for England, 2017, ICD 10 code C91.1
[2] Company submission
[3] Clinical expert opinion

Assumptions

4.2 The resource impact template assumes that:

- people with a 17p deletion or TP53 mutation (untreated) are currently treated with ibrutinib as a first-line treatment
  - in year 1, 5% of this group of people will be treated with acalabrutinib, 7.5% with venetoclax plus obinutuzumab and 87.5% with ibrutinib. From year 5 onwards, 55% of this group of people will be treated with acalabrutinib, 30% with venetoclax plus obinutuzumab and 15% with ibrutinib.

- around 10% of people with no 17p deletion or TP53 mutation (untreated who are not fit for treatment with FCR/BR) are currently treated with venetoclax plus obinutuzumab as a first-line treatment
  - in year 1, 40% of this group will be treated with acalabrutinib, 30% with venetoclax plus obinutuzumab and 30% with obinutuzumab plus chlorambucil. From year 4 onwards 85% of this group of people will be treated with acalabrutinib ,10%

with venetoclax plus obinutuzumab and 5% with obinutuzumab plus chlorambucil.

- In people with a 17p deletion or TP53 mutation (treated) who receive a first-line treatment of ibrutinib, 12% will receive second-line treatment in year 2 and 20% of people will receive it in year 3.
- In people who receive a 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.
- In people who receive a first-line treatment of acalabrutinib, 10% will receive second-line treatment in year 2 and 30% of people will receive it in year 3.

- In people without a 17p deletion or TP53 mutation (treated) who receive a first-line treatment of obinutuzumab plus chlorambucil, 9% will receive second-line treatment in year 2 and 29% of people will receive it in year 3
- In people who receive a first-line treatment of venetoclax plus obinutuzumab, 5% will receive second-line treatment in year 2 and 10% of people will receive it in year 3.
- In people who receive a first-line treatment of acalabrutinib, 10% will receive second-line treatment in year 2 and 15% of people will receive it in year 3.
- In people who receive a first-line treatment of FCR or BR, 9% will receive second-line treatment in year 2 and 29% of people will receive it in year 3

<u>First-line treatments</u>

<u>Acalabrutinib</u>

- the dose of acalabrutinib is
  - 100 mg twice daily

  - each cycle is 30 days long and it is assumed that there are 36 cycles. The medication is taken orally at home.
- All cycles of treatment are covered by SB11Z Deliver Exclusively Oral Chemotherapy which has a tariff of £127 per attendance (National tariff 20/21).

The dose of venetoclax plus obinutuzumab is:

Venetoclax

  - 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.

Obinutuzumab

  - 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).

Chlorambucil

- 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

- ibrutinib is taken daily at a dose of 1 420mg tablet. 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 £127 per attendance (National tariff 20/21).

Second-line treatments

Acalabrutinib

- the dose of acalabrutinib is a second-line treatment is the same as listed above in first-line treatments.

Ibrutinib

- in second-line treatment ibrutinib is taken at a dose of 1 420mg tablet. The 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

- 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 to 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 acalabrutinib 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 Acalabrutinib for treating chronic lymphocytic leukaemia and should be read with it.