NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Arsenic trioxide for treating acute promyelocytic leukaemia (TA526)

Published: June 2018

Summary

NICE has recommended arsenic trioxide for as an option for induction of remission, and consolidation in acute promyelocytic leukaemia (characterised by the presence of the t[15;17] translocation and/or the PML/RAR-alpha gene) in adults. We estimate that:

- 150 people with acute promyelocytic leukaemia, and are low to intermediate risk patients, are eligible for first line treatment with arsenic trioxide
- 135 people will have first line treatment with arsenic trioxide from year 2019/20 onwards once uptake has reached 90%.
- 10 people will have second line treatment with arsenic trioxide following a relapse after having all-trans retinoic acid (ATRA) and chemotherapy.

The estimated annual cost of implementing this guidance for the population of England based on the uptake in the resource impact assumptions is shown in table 1.

Table 1 Estimated annual cost of implementing the guidance in England

	2018/19	2019/20	2020/21	2021/22	2022/23
Estimated market share for arsenic trioxide (%)	30	90	90	90	90
Population having arsenic trioxide each year	50	145	145	145	145
Total resource impact (£000)	**1,100**	**8,900**	**8,900**	**8,900**	**8,900**

This report is supported by a resource impact template which may be used to calculate the resource impact of implementing the guidance by amending the variables.

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

1 Arsenic trioxide

1.1 NICE has recommended arsenic trioxide, within its marketing authorisation, as an option for induction of remission, and consolidation in acute promyelocytic leukaemia (characterised by the presence of the t[15;17] translocation and/or the PML/RAR-alpha gene) in adults with:

- untreated, low-to-intermediate risk disease (white blood cell count 10 x 10^3/microlitre or less), when given with all-trans-retinoic acid (ATRA)
- relapsed or refractory disease, after a retinoid and chemotherapy.

1.2 Acute promyelocytic leukaemia (APL) is a rapidly progressing form of leukaemia for which treatment must be started quickly. Symptoms include bruising or bleeding, fatigue, feeling weak or breathless, bone or joint pain and sleeping problems.

1.3 Current treatments have high toxicity. For example, the long-term effects of chemotherapy can include a risk of secondary cancers and loss of fertility in younger people.

1.4 Current treatment for untreated, low-to-intermediate risk APL is ATRA with an anthracycline-based chemotherapy (usually idarubicin, a combination known as AIDA).

1.5 Arsenic trioxide (ATO) plus ATRA is the current standard of care for second line treatment of APL.

1.6 Clinical trial evidence shows that ATO plus ATRA is effective for untreated disease when compared with AIDA.

2 Resource impact of the guidance

2.1 We estimate that:

- 150 people in England with APL, and are low to intermediate risk patients, are eligible for treatment with arsenic trioxide each year.

- 135 people will have arsenic trioxide as first line treatment from year 2019/20 onwards once uptake has reached 90%.

- 10 people will have arsenic trioxide as second line treatment following a relapse after having ATRA and chemotherapy.

2.2 The current treatment and future uptake figure assumptions are based on the company budget impact submission and are shown in the resource impact template.

2.3 The estimated annual cost of implementing this guidance for the population of England based on the uptake in the resource impact assumptions is shown in table 2. The cost from year 2019/20 once steady state is reached is equivalent to £16,200 per 100,000 population.

Table 2 Resource impact of implementing the guidance using NICE assumptions

	2018/19	**2019/20**	**2020/21**	**2021/22**	**2022/23**
Estimated market share for arsenic trioxide (%)	30	90	90	90	90
Population having arsenic trioxide each year	50	145	145	145	145
Total resource impact (£000)	**1,100**	**8,900**	**8,900**	**8,900**	**8,900**

2.4 This report is supported by a resource impact template which may be used to calculate the resource impact of implementing the guidance by amending the variables.

Savings and benefits

2.5 Arsenic trioxide has been available as a treatment for relapsed or refractory APL patients for over 15 years, but its true innovative potential lies in offering a chemotherapy-free treatment option to newly-diagnosed low- to intermediate-risk APL patients, allowing them to avoid short- and long-term toxicity associated with chemotherapy.

3 Implications for commissioners

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

3.2 Arsenic trioxide will be available through routine commissioning.

3.3 Arsenic trioxide falls within the programme budgeting category 02I: Cancer, Haematological.

4 How we estimated the resource impact

The population

4.1 The annual incidence of people with acute myeloid leukaemia (AML) is around 2,700 (Acute myeloid leukaemia (AML) statistics - Cancer Research UK). Around 7% are of cases of APL (Company submission). Table 3 shows the details of the population with APL who are estimated to be eligible for treatment with arsenic trioxide.

Table 3 Number of people eligible for treatment in England

Population	Proportion of previous row (%)	Number of people
Total population		54,786,327
Adult population		43,108,471
Incidence of acute myeloid leukaemia (AML)[1]	0.01	2,700
Proportion with acute promyelocytic leukaemia (APL)[2]	7.4	200
Proportion of low to intermediate risk patients[2]	75.7	150
Proportion of high risk patients[2]	24.3	50
Population expected to have ATO + ATRA at first line from 2019/20 (90% x 150)	90	135
Low to intermediate risk patients having AIDA first line[2] (10% x 150)	10	15
High risk patients having AIDA first line[2] (100% x 50)	100	50
People having AIDA (15+50)		65
People having ATO + ATRA with relapsed disease[3] (17.5% x 65)	17.5	10
Population expected to have ATO + ATRA at second line from 2019/20		10

[1] Acute myeloid leukaemia (AML) statistics - Cancer Research UK

[2] Company submission

[3] Zi-Jie Long, et al 2014. ATO/ATRA/Anthracycline-Chemotherapy Sequential Consolidation Achieves Long-Term Efficacy in Primary Acute Promyelocytic Leukemia

Assumptions

4.2 The resource impact template assumes that:

- Based on the company submission, 90% of people with APL, and are low to intermediate risk patients, are expected to receive treatment with arsenic trioxide at first line.
- Based on the company submission, 135 people will be treated with arsenic trioxide at first line, from year 2 onwards, once a steady state is reached.
- The relapse rate of 17.5%, of patients receiving AIDA, is

taken from: Zi-Jie Long, et al 2014. ATO/ATRA/Anthracycline-Chemotherapy Sequential Consolidation Achieves Long-Term Efficacy in Primary Acute Promyelocytic Leukemia.

- 10 people who relapse after having AIDA will be treated with arsenic trioxide at second line.
- Clinical expert opinion is that the relapse rate for people being treated under the ATO combined with ATRA regimen is very low. It is assumed people will not require second line treatment after receiving ATO combined with ATRA.
- Arsenic trioxide has been approved in the relapsed/refractory APL setting for the last 15 years and is considered the current standard of care for second-line APL treatment in the UK.
- The national tariff costs for delivering complex Chemotherapy at first attendance, and subsequent attendances has been used for all the treatments.
- During the induction phase, patients require particularly close monitoring and are generally hospitalised, whether they receive ATO- or chemotherapy-based treatment. During consolidation, however, patients are able to receive treatment with ATO primarily in the day-care setting, unless otherwise indicated. During the consolidation phase ATO requires more frequent dosing than chemotherapy (80 infusions as opposed to 10 in the AIDA regimen) (page 11 of company submission).
- The dosage regimen for ATRA+ATO is taken from the company submission (reference: Lo-Coco F, et al. Retinoic acid and arsenic trioxide for acute promyelocytic leukemia, 2013).
- The dosage regimen for arsenic trioxide is taken from the company, summary of product characteristics.

About this resource impact report

This resource impact report accompanies the NICE guidance on arsenic trioxide for treating acute promyelocytic leukaemia and should be read with it.