Review of TA524; Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma

TA524 was published in June 2018 and scheduled to be considered for review in 2021.

Decision

1. TA524 remains relevant and an update is not needed.

Rationale

2. Since the publication of TA524 18 articles have been published relating to the conclusions of TA524. Much of this new evidence reports new survival data and analyses. The majority is generalisable to the UK. No major safety concerns have been raised. Because the findings of these new articles support the committee's conclusions from TA524, and there is no new evidence to address the key uncertainties in population at increased risk of relapse or progression after autologous stem cell transplant (population 2; not recommended), there is no need to undertake a full review of the guidance. We are unaware of any new evidence being published in the next few years which would make the deferral of the review decision appropriate. There are no ongoing clinical guidance updates to which this guidance should be cross-referred. It is recommended that this guidance remains relevant and an update is not needed.

Summary of new evidence and implications for review

Has there been any change to the price of the technology(ies) since the guidance was published?

3. No, price unchanged.

Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?

4. The marketing authorisation has been expanded to include "ADCETRIS is indicated for adult patients with previously untreated CD30+ Stage IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD) (see sections 4.2 and 5.1)." This does not affect the existing guidance, but an appraisal for this new population would be appropriate.

Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?

5. Estimates of survival, health-related quality of life, and relative rates of stem cell transplants after chemotherapy or brentuximab vedotin were the key uncertainties in the original guidance.

6. A UK and German real-world data study (2018) found people who received brentuximab vedotin after ASCT had better survival than people received chemotherapy. Another UK study (2020) in people with relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL) after autologous stem cell transplantation (ASCT), found 5-year survival was higher for people taking brentuximab vedotin (92.2%) than those people receiving salvage chemotherapy (30.5%). Similar statistically significant benefits favouring brentuximab were also found when considering progression free survival. 5-year follow-up from the trial (AETHERA) in people at increased risk of relapse after ASCT has been published. It found that consolidation with brentuximab vedotin after ASCT improved progression free survival compared to placebo. Another study found using brentuximab vedotin or a 2nd SCT after 2 failed therapies (population 3) could improve survival. While this newly available evidence may address some of the previously highly uncertainties relating to survival, the findings are supportive of the committee's original considerations and conclusions relating to the original evidence base. So, it is unlikely this evidence would change the original recommendation.

7. No new evidence has been published which would address uncertainties relating to long-term health related quality of life in people with CD30+ Hodgkin's

Lymphoma at increased risk of relapse or progression after autologous stem cell transplant.

8. Uncertainties relating to relative rate of post-chemotherapy and post-brentuximab vedotin stem cell transplants were addressed through data collection in the CDF. No other evidence has been published in this area.

9. Safety analysis from AETHERA (2018) found adverse events from brentuximab consolidation after ASCT to be manageable and reversible.

Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?

10. Since the publication of TA446 (original before TA524 CDF review) NICE has published other pieces of guidance for Hodgkin's Lymphoma (TA462, TA540, TA594). The recommendation of this proposal paper does not have any implications for those other pieces of guidance.

Additional comments

11. The search strategy from the original ERG report (2016) was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from January 2018 to February 2021 were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above.

Equality issues

12. No potential equalities issues were raised in the original piece of guidance.

Decision paper sign off

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Appendix A – Information from existing guidance

Original remit

To appraise the clinical and cost effectiveness of brentuximab vedotin (Adcetris) within its licensed indication for treating CD30-positive Hodgkin lymphoma in adults.

Current guidance

1.1 Brentuximab vedotin is recommended as an option for treating CD30-positive Hodgkin lymphoma in adults with relapsed or refractory disease, only if:

- they have already had autologous stem cell transplant or
- they have already had at least 2 previous therapies when autologous stem cell transplant or multi-agent chemotherapy are not suitable and
- the company provides brentuximab vedotin according to the commercial arrangement.

1.2 These recommendations are not intended to affect treatment with brentuximab vedotin 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.

Research recommendations from original guidance

N/A

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the specify STA or MTA process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to specify date or trial.	NICE will reconsider whether a review is necessary at the specified date.	No
The guidance should be Cross referred into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance remains relevant until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance remains relevant and an update is not needed.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Appendix C

Relevant Institute work

Published

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma (2018) NICE technology appraisal guidance 540.

Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma (2017)) NICE technology appraisal guidance 462.

In progress

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 1 prior therapy. NICE technology appraisal guidance. Publication expected June 2021.

Details of changes to the marketing authorisation for the technology

Marketing authorisation and price considered in original appraisal

Brentuximab vedotin (Adcetris) is indicated for treating relapsed or refractory CD30-positive Hodgkin lymphoma in adults:

- after autologous stem cell transplant or
- after at least 2 prior therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option
- at increased risk of relapse or progression after autologous stem cell transplant.

Active ingredients	Size	NHS indicative price
Brentuximab vedotin 50 mg	1	£2500.00

Current marketing authorisation (for this appraisal) and current price

The marketing authorisation has been expanded. It now includes an additional population. The NHS indicative price is the same.