National Institute for Health and Care Excellence

Health Technology Evaluation

Obecabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia ID6347
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Autolus (company)	This is an appropriate topic for NICE to consider as a single technology appraisal. Acute lymphoblastic leukaemia (ALL) survival outcomes differ depending on age and treatment response, with considerably poorer outcomes in older and relapsed patients. There is a high unmet need for an effective treatment with less toxicity suitable for all adult R/R patients with B-cell ALL.	Thank you for your comment. No changes to the scope required.
Wording	Autolus (company)	Autolus anticipate that the marketing authorisation will be for [redacted]. As such, please amend the wording to: "To appraise the clinical and cost effectiveness of obecabtagene autoleucel within its marketing authorisation for treating [redacted] *with* relapsed or refractory B-cell acute lymphoblastic leukaemia."	Thank you for your comment. Because marketing authorisation wording may be subject to change, it is appropriate to keep the remit broad. The remit of the scope has been amended to "appraise the clinical and cost

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			effectiveness of obecabtagene autoleucel within its marketing authorisation for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in adults."
Timing issues	Autolus (company)	A timely evaluation of obe-cel will ensure that eligible patients with high unmet need will have access at the earliest opportunity.	Thank you for your comment. NICE has scheduled this topic into its work programme. For further details, please see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11496. No changes to the scope required.
	Anthony Nolan	This is a timely evaluation as at present there is only one other CAR-T product available for this indication and alternative options that can offer reduced toxicity and longer persistence are urgently required	Thank you for your comment. Thank you for your comment. NICE has scheduled this topic into its work programme. For further details, please see the NICE website:

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			https://www.nice.org.uk/guidance/indevelopment/gid-ta11496. No changes to the scope required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Autolus (company)	**Current wording**: "ALL is more common in than women." **Suggested wording**: "ALL is more common in ***men*** than women" **Rationale**: Typo. **Current wording: "**There is no universally accepted treatment approach for relapsed or refractory ALL. Treatment may include conventional combination chemotherapy and for most people this would be fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG) with idarubicin" **Suggested wording:** "As per European Society for Medical Oncology (ESMO) guidelines, B-cell ALL adults who face relapse receive immunotherapy (Philadelphia chromosome negative [Ph-] patients) or tyrosine kinase inhibitor (TKI)-immunotherapy + chemotherapy (Ph positive [Ph+] patients). Current treatments in the UK for adult R/R B-cell ALL include tisagenlecleucel (for patients aged < 26 years), blinatumomab (for Ph- patients), ponatinib (for Ph+ patients) and inotuzumab ozogamicin."	Thank you for your comment. The scope has been amended to state that "ALL is more common in *men* than women." The current treatments in the suggested wording are referenced later in the background section as treatments recommended by NICE. Current clinical guidelines suggest that FLAG-based chemotherapy remains a treatment option for

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		Rationale: Referring to treatments currently available being used in UK clinical practice. **Current wording: "**Obecabtagene autoleucel (brand name unknown, Autolus) does not currently have a marketing authorisation in the UK for treating relapsed or refractory B-cell ALL. It has been studied in a clinical trial in adults aged 18 years and over with relapsed or refractory B-cell ALL." **Suggested wording:** "Obecabtagene autoleucel (brand name unknown, Autolus) does not currently have a marketing authorisation in the UK for treating relapsed or refractory B-cell ALL. ***The anticipated marketing authorisation is for [redacted] with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia.*** It has been studied in a clinical trial in adults aged 18 years and over with relapsed or refractory B-cell ALL." **Rationale:** Adding anticipated marketing authorisation for clarity.	some adults with relapsed or refractory ALL, so reference to FLAG-based chemotherapy as a treatment for relapsed or refractory ALL has been retained, please see response to comment in "comparators" section. The anticipated marketing authorisation wording is not included in the scope since it may be subject to change. The current wording in the technology section of the scope has been retained.
Population	Autolus (company)	Yes.	Thank you for your comment. No changes to the scope required.

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Subgroups	Autolus (company)	No subgroups are anticipated to be considered separately	Thank you for your comment. No changes to the scope required.
Comparators	Autolus (company)	According to the anticipated place of obe-cel in the treatment pathway, the appropriate comparators are as follows: • Inotuzumab ozogamicin • Blinatumomab (Ph-) • Ponatinib (Ph+) The following therapies should not be in scope based on the final licence wording for obe-cel: • Tisagenlecleucel • Clofarabine Obe-cel's expected indication is [redacted]. Tisagenlecleucel is recommended as an option for people 25 years and under, and clofarabine is not recommended but possibly used off-label in young adults. The following therapy lies within the licence of obe-cel, but evidence will not be presented against it due to the positioning of obe-cel alongside clinical feedback and committee preferences expressed in TA893: • FLAG-based chemotherapy	Thank you for your comment. The scope has been amended to remove clofarabine and stem cell transplantation as comparators. Because the marketing authorisation wording may be subject to change, tisagenlecleucel has been kept in the scope as a comparator for people aged 25 years and under so as not to exclude a potentially relevant comparator. The scope is intended to be broad, so as not to exclude potentially relevant comparators.

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		Based on clinical feedback, ESMO guidelines, and committee preference in TA893 (brexucabtagene autoleucel [brexu-cel] for treating R/R B-cell ALL in people 26 years and over), FLAG-IDA is not relevant in this population. In TA893, the committee had concerns of the toxicity associated with FLAG-IDA, and the limited use in clinical practice. The patients anticipated to receive obe-cel are equally fragile than those receiving brexu-cel. Therefore, it is unlikely that obe-cel's population would be eligible for FLAG-IDA. This view was shared by two clinical experts interviewed as part of this submission. The following therapy should not be included as comparator in the scope as it is for an earlier line of treatment not included within the licence: • Imatinib Imatinib is used earlier in the treatment pathway and is therefore not a relevant comparator to obe-cel. Obe-cel is anticipated to be used in adults with R/R B-cell ALL who have had at least two prior lines of therapy. The following therapy should not be included as comparator in the scope as it is not reimbursed in the UK and not used in clinical practice. • Dasatinib The following therapy should not be included as comparator in the scope as it is considered an outcome following therapeutic treatment. • Stem cell transplantation (SCT)	Current clinical guidelines suggest that FLAG-based chemotherapy remains a treatment option for some adults with relapsed or refractory ALL. Imatinib, dasatinib and ponatinib are also recommended in clinical guidelines for relapsed or refractory Philadelphia chromosome-positive ALL, with the choice of tyrosine kinase inhibitor depending on a person's previous treatment and T315I gene mutation status. Therefore, FLAG-based chemotherapy, imatinib and dasatinib have been retained as comparators in the scope.

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		The rate of subsequent SCT is an outcome rather than a comparator. This is evidenced by its inclusion as an outcome in this draft scope and not a comparator in the TA893 scope. Considering that obe-cel's positioning is aligned with that of brexu-cel, SCT is consequently not a relevant comparator to obe-cel. The following therapy lies within the licence of obe-cel, but evidence will not be presented against it due to the positioning of obe-cel: Best supportive care Best supportive care (palliative care) would be given to patients who cannot tolerate chemotherapies or targeted treatments. Therefore, these patients would not be eligible for CAR-T therapy and therefore best supportive care is not a relevant comparator to obe-cel.	
Outcomes	Autolus (company)	Yes.	Thank you for your comment. No changes to the scope required.
Equality	Autolus (company)	There are no known equality issues relating to the use of obe-cel in patients with B-cell ALL.	Thank you for your comment. No changes to the scope required.
Other considerations	Autolus (company)	There are no additional issues to comment on.	Thank you for your comment. No changes to the scope required.

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Questions for consultation	Autolus (company)	*Where do you consider obecabtagene autoleucel will fit into the existing care pathway for relapsed or refractory B-cell acute lymphoblastic leukaemia?* **Answer:** Obe-cel is anticipated to be used in [redacted] with R/R B-cell ALL who have had at least two prior lines of therapy. *Is off-label use of clofarabine in young adults part of current care for relapsed or refractory B-cell acute lymphoblastic leukaemia? If so, up to what age would clofarabine be used?* **Answer:** Not relevant due to expected marketing authorisation. According to an expert consulted for TA893, clofarabine-based chemotherapy is not used in clinical practice in the UK for the population and has never been approved in adult R/R ALL. *Please select from the following, will obecabtagene autoleucel be:* *A. Prescribed in primary care with routine follow-up in primary care* *B. Prescribed in secondary care with routine follow-up in primary care* *C. Prescribed in secondary care with routine follow-up in secondary care* *D. Other (please give details):* **Answer:** C. *For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.* **Answer:** The setting does not differ for comparators.	Thank you for your comment. The scope has been amended to remove clorafabine from the list of comparators.

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		Would obecabtagene autoleucel be a candidate for managed access? **Answer:** Yes. *Do you consider that the use of obecabtagene autoleucel can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?* **Answer:** No.	
Additional comments on the draft scope		No comments	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

Novartis Pharmaceuticals UK