National Institute for Health and Clinical Excellence

Table of responses to C&C comments on draft scope

Temsirolimus for the treatment of mantle cell lymphoma

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	BOPA	There is no standard therapy for 1st or 2nd line treatment for MCL; it is difficult therefore to understand the place in therapy of temsirolimus. A negative opinion may have little effect on treatment, a positive opinion may lead to a treatment being recommended which has not been compared to other available regimens.	Comment noted. The technology will be appraised within its licensed indication.
	Lymphoma association	No comment	Comment noted
	Wyeth	The incidence of MCL is very small (approx. 500 new cases in the UK per year), and the patient population studied for treatment with Torisel is a subset of that - relapsed/refractory MCL, majority are Stage IV. Therefore the disease is ultra-orphan and together with all other current and anticipated indications for temsirolimus it will still remain an ultra-orphan drug. Given that the decision rules employed by NICE are unsuitable for the appraisal of ultra-orphan drugs it would be inappropriate to refer this topic to NICE.	Comment noted
Wording	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	No comment	Comment noted
Timing Issues	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	No comment	Comment noted
Additional comments on the draft remit	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted

Section	Consultees	Comments	Action
	Wyeth	MCL is an ultra-orphan disease and temsirolimus is an ultra-orphan drug even when all its current and anticipated indications are taken into account. An appraisal of a disease and a drug of a very limited impact on the NHS budget may thus be inappropriate use of NICE resources.	Comment noted

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	BOPA	The background makes no mention of best supportive care. Some patients may progress slowly and be managed using BSC alone.	The background section has been amended following consultation on the scope.
	Lymphoma association	Although accurate on the whole, this section fails to make explicit the real difficulties for the majority of people with mantle cell lymphoma. After relapse, most people will experience a variety of unpleasant therapies, often of increasing toxicity, at increasingly regular intervals, with increasingly poor response rates. The many therapies cited, and the acknowledged lack of consensus on standard therapy, are an indication of the conundrum that this disease presents to clinician and patient. Mantle cell lymphoma is also the subject of many other investigations of new therapies, or potential new applications of therapies with activity in other cancers. Clinicians and patients are anxious for any potential improvement in the management of this disease, which currently offers a bleak outlook for those newly diagnosed.	Comment noted. The background section of the scope is intended to be a brief overview, see section 2 of the Guide to the Methods of Technology Appraisal. http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp?domedia=1&mid=B52851A3-19B9-E0B5-D48284D172BD8459 Comment noted.
	Wyeth	No comment	Comment noted

Section	Consultees	Comments	Action
The technology/ intervention	BOPA	Temsirolimus needs to be given as a once weekly infusion	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	No comment	Comment noted
Population	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	Population would be predominantly those with Stage IV disease so just a subset of all MCL patients.	Comment noted. At the scoping workshop consultees agreed that specifying the population further to state patients with stage IV disease was not necessary.
Comparators	BOPA	No particular regimen can be described as best alternative care. Subsequent treatment will depend on a variety of factors including previous treatments, feasibility of autograft, symptoms	Comment noted. Specific comparators could not be determined at the scoping workshop. Consultees at the workshop agreed that BSC should be included in the scope in addition to a range of treatment regimens that may include gemcitabine and fludarabine.

Section	Consultees	Comments	Action
	Lymphoma association	There is no consensus on alternative care, so the wording of the draft scope will cover the many potential comparators for patients with relapsed or refractory disease.	Comment noted. Specific comparators could not be determined at the scoping workshop. Consultees at the workshop agreed that BSC should be included in the scope in addition to a range of treatment regimens that may include gemcitabine and fludarabine.
	Wyeth	There is currently no standard of care in Europe. The comparator in the Phase III trial was investigator's choice of treatment. Best supportive care is not an appropriate comparator since MCL patients tend to be given numerous lines of treatment.	Comment noted. Specific comparators could not be determined at the scoping workshop. Consultees at the workshop agreed that BSC should be included in the scope in addition to a range of treatment regimens that may include gemcitabine and fludarabine.
Outcomes	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	No comment	Comment noted
Economic analysis	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted

Section	Consultees	Comments	Action
	Wyeth	No comment	Comment noted
Other considerations	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	No comment	Comment noted
Questions for consultation	BOPA	Subject to the available evidence, possible comparators could be best supportive care (in patients for whom chemotherapy is inappropriate) or physician's choice of active treatment for other cases. It is unclear which chemotherapy regimens are used routinely; there is the LY05 trial which compares FC vs. R-FC. However, rituximab may already be considered by some to be part of standard treatment. Radiotherapy may not always be considered appropriate as these patients may have stage IV disease. Radiotherapy for symptom relief could be considered as part of BSC.	Comment noted. Specific comparators could not be determined at the scoping workshop. Consultees at the workshop agreed that BSC should be included in the scope in addition to a range of treatment regimens that may include gemcitabine and fludarabine.

Section	Consultees	Comments	Action
	Lymphoma association	What are the appropriate comparators to temsirolimus for the treatment of relapsed or refractory mantle cell lymphoma? Which single and combination treatment regimens are used routinely in clinical practice? as above Is radiotherapy an appropriate comparator for people who have relapsed or are refractory to prior therapies? Radiotherapy alone is less likely to be used with the intention to achieve remission. It can be used in the context of high dose therapy and stem cell transplant, or for local control of enlarged nodes for palliation. Is best supportive care (i.e. no active treatment) an appropriate comparator? If so, how should best supportive care be defined? As patients opting for temsirolimus will be those in need of - and seeking - active treatment, it may be difficult to find trial data comparing this therapy with best supportive care. Existing data compares temsirolimus with a variety of other treatments. Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality? As with all cancer treatment appraisals, mantle cell lymphoma is largely a disease of later life and many of the patients in question will be ineligible for comparative therapies. The implications for equal access to potential cancer treatments for older people should be considered. Which process would be the most suitable for appraising this technology, the single technology or multiple technology process? STA process.	Comment noted. Specific comparators could not be determined at the scoping workshop. Consultees at the workshop agreed that BSC should be included in the scope in addition to a range of treatment regimens that may include gemcitabine and fludarabine.
	Wyeth	No comment	Comment noted
Additional comments on the draft scope.	BOPA	No comment	Comment noted
	Lymphoma association	No comment	Comment noted
	Wyeth	No comment	Comment noted

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

NHS Quality Improvement Scotland
National Public Health Service (Wales), (NPHS)
Royal Pharmaceutical Society
GlaxoSmithKline
Royal College of Nursing (RCN)
Welsh Assembly Government