

Appraising end of life medicines

Public consultation comments

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Issues for consideration	Comments
<p>What is your view on the proposition that the Committee should be asked to place additional weight on proven survival benefits in patients with terminal illness and short life expectancy.</p>	<p>The International Brain Tumour Alliance (IBTA) welcomes this consultation on raising the QALY ceiling in relation to end of life medicines, and appreciates the opportunity to respond to this initiative.</p> <p>There are over 120 different types of primary brain tumours. Unlike many other cancers, primary brain tumours affect people of any age, from tiny babies to the elderly. The causes of brain tumours are largely unknown so there are no prevention programmes for them nor any realistic screening programmes. There is no known preventative option by healthy living, diet or exercise.</p> <p>So it falls to new, promising therapies to provide the only hope for this patient group. Because treatment options are currently so limited for brain tumours, it is vital that patients have every chance to access promising, cutting-edge therapies which although they may not save life, can</p>

	<p>provide extended survival with a good quality of life.</p> <p>The cumulative effects of the brain tumour journey on patient, family and caregiver are extremely traumatic because of the very location of the tumour and its wide-ranging consequences on both the mental and physical capacity of the patient – something that happens with no other cancer.</p> <p>It is against this background that a much more flexible mechanism needs to be put in place by NICE in terms of appraising end of life medicines such as those for brain tumours. We were extremely disappointed when NICE did not accept its Citizens Council recommendation on the Rule of Rescue inquiry, but heartened to learn NICE feels that, overall, there is a place for Social Value Judgements in the appraisal process, such as considering severity as an important factor. We would also highlight the importance of the caregiver’s role in this equation and the economic contribution that caregivers provide which shouldn’t be underestimated.</p> <p>Special weight should definitely be given to life extending medicines which offer proven survival benefits. It is crucial to raise the QALY ceiling to accommodate these types of therapies. For diseases such as brain tumours – where there is a relatively small population - i.e. only about 1800 patients are diagnosed annually in the UK with highly malignant glioblastoma multiforme (GBM) brain tumours - the overall cost of treatment will be smaller so therefore a higher threshold for the QALY is appropriate.</p> <p>Rare and less common cancers with small patient populations, such as brain tumours, present a complicated situation. Pharmaceutical companies may not be interested in developing new therapies for patients with a rare disease because their return will be limited. There are fewer opportunities for clinical trials due to a smaller overall cohort of available patients who will participate as trial subjects. Because of the rarity of the disease, optimal treatment approaches are not always evident and there may be controversy over the best way forward. Initiatives are certainly needed to strongly encourage investment in producing a new wave of promising, innovative, targeted and combination therapies.</p>
<p>Is the wording in section 2, in particular, appropriate and will it help the Appraisal Committees achieve the objective set out in section 1.</p>	<p>With regard to the wording in section 2, many points require further clarification before determining whether the wording will help the Appraisal Committees to achieve the objects set out in Section 1.</p> <p>We are concerned about the lack of detail in the consultation document and also some of the terminology used (see relevant sections below).</p>

Summary statements – there seems to be no mention of how the cost of expensive targeted treatments will be incorporated into the thinking or how important, emerging combination therapies will be accommodated. Current practice in the treatment of brain tumours, for example, is focusing strongly on a multi-modal approach.

Regarding **Summary statement 1.3** which cites: “The population for which the medicine is indicated and licensed should not normally exceed 7,000...” and **Criteria statement 2.1.1** which says: “The medicine is indicated, in its licence, for a patient population normally not exceeding 7,000 new patients per annum.” The method of determining a population figure of 7,000 needs to be explained. It is not clear where this figure comes from or what the epidemiological basis for this figure is although with regard to brain tumours, we assume that all those in this generally described patient population will be adequately covered (i.e. there are 1800 patients diagnosed annually with the highly aggressive glioblastoma multiforme (GBM) brain tumour and similar examples of discrete statistical groupings of small size diagnosed with one of the other 120+ types of brain tumour which exist).

Additionally in **Summary statement 1.5**, it is noted that “Each candidate medicine will need to meet a set of criteria (see section 2). The Appraisal Committee will apply these criteria as an addendum to section 6.2.25 of the Guide to the Methods of Technology Appraisal and will formulate recommendations accordingly.” Section 6.2.25 was in operation during NICE’s appraisal of the brain tumour therapy temozolomide for newly diagnosed GBM which, despite forming part of standard care in much of the developed world, was rejected by NICE. The decision was later overturned and the therapy was ultimately approved for reimbursement on the NHS. Perhaps the Guide to the Methods of Technology Appraisal should also be reviewed and updated in light of experiences such as this.

With regard to the Criteria listed in **Section 2**:

(a) **Section 2.1.2**. The point in time at which a disease is diagnosed as a “terminal illness” is not clearly stated and needs to be defined. With regard to the criteria “...who are not, on average, expected to live for more than 24 months...” how does this relate to newly diagnosed patients? How does it relate to the recurrent disease setting? Additionally, what would be the situation with a “pre-malignant” condition such as a diagnosis of low grade glioma? This type of so-called “benign” brain tumour can also be considered “terminal” because the majority of low grade gliomas progress over time to become highly malignant and ultimately lethal. The period of time to malignancy can

	<p>vary greatly. These complications when considering the meaning of “terminal” point to the necessity for a more disease-specific approach in determining a QALY ceiling.</p> <p>(b) Section 2.1.3 – this is perhaps one of the most controversial aspects of the criteria set out in the consultation document. The term “substantial extension to life” is extremely subjective. This needs to be better defined. Would this, for example, equate with a few months or would it be a percentage improvement in survival? “Substantial extension to life” means different things to different people at different stages of their brain tumour journey. Many brain tumour patients would feel that even a few months’ extension of life is “substantial”, given their overall prognosis for a vastly shortened life. Having an extra two months when you were originally expected to survive for four months for example is, after all, a 50% increase in survival – “substantial” enough?</p> <p>(c) Section 2.2.1 – what is the definition of “the extension to life” in this section and also in section 2.3? This is clearly a key phrase, the definition for which it is crucial to clarify.</p> <p>Other comments:</p> <p>(d) How would this new overall approach on end of life medicines described in the consultation document affect any appeals processes for therapies initially rejected by the NICE Appraisal Committees?</p> <p>(e) Overall, the criteria in Section 2 seem to focus quite heavily on proof of mortality rather than also considering in more detail the importance of therapies - including targeted and combination treatments - which provide significant improvements in morbidity and/or quality of life.</p>
<p>Are there valid alternative methods which might be used to achieve the same ends, in the short or the long term.</p>	<p>We are not health economists so cannot provide alternative specific formulae. But it seems sensible to assume that in any one patient population in which it is possible to determine the number of patients likely to need access to a particular therapy, this could determine affordability. It is of course vital to have equity across an entire range of diseases but, as NICE has indicated earlier in the Summary Section of the document, other elements such as severity of disease should be taken into account as well as a therapy’s positive effects on morbidity and/or quality of life.</p> <p>It goes without saying that any alternative methods which are applied to health technology assessments should be fair, flexible, transparent and take into account a range of issues not</p>

	currently covered by the QALY, so that patients who desperately need vital treatments can access them.
General comments on the proposal	<p>We also wonder about the actual title of the consultation “Appraising End of Life Medicines”. One might not necessarily call some of the expensive brain tumour therapies in development “end of life medicines” but nevertheless, there are situations where patients must be able to access these vital cutting-edge therapies although they have not yet necessarily reached “end of life”. We wonder too if instead of using the word “medicines”, a broader description should be used such as “therapies” or “treatments” which allows consideration of innovative medical devices which might also be applied in an “end of life” situation and which involve additional monitoring costs. We can think of an example of a brain tumour treatment device currently in clinical trials in the United States when such a situation could arise.</p> <p>Additionally, although it may be outside of the scope of this appraising end of life medicines document, we would like to make a procedural point. We ask NICE to ensure that on every Appraisal Committee evaluating new therapies, particularly for rare and less common cancers like brain tumours, there should be at least one specialist clinician with substantial experience and expertise of the relevant disease (or grouping of diseases) for which the appraised therapy is being considered.</p>