Steve Brine MP
Chair, Health and Social Care Select Committee
House of Commons
London
SW1A 0AA

23 April 2024

Dear Chairman,

We committed to keeping you updated on the status of the NICE appraisal of trastuzumab deruxtecan (ENHERTU▼) for use in patients with HER2-low metastatic breast cancer (approximately 1,000 patients per year across England).

As you are aware, NICE issued final draft guidance (5th March 2024) not to recommend this medicine for use on the NHS in England. This draft guidance is due to be finalised on 15th May 2024. For reference this medicine has been available for routine use in Scotland since December 2023 after the Scottish Medicines Consortium (SMC) concluded it represented a clinically effective and cost-effective use of NHS resources.

Daiichi Sankyo and AstraZeneca are extremely disappointed by, and disagree with, NICE's decision. We acknowledge the anxiety, frustration and distress felt by those patients, families and loved ones who will be most affected by this outcome. We are keen to explain, as transparently as possible, why this outcome has happened. This requires we set out some background context and a brief explanation of the complexities in how these decisions are reached, hence this relatively detailed letter.

We believe NICE's decision to be a direct result of the change to the formula for appraising medicines (as set out in the NICE new combined methods and processes manual, January 2022). The 'end-of-life criteria', originally introduced in 2009, provided the flexibility of an extra value weighting for some treatments that are used to treat patients with terminal illnesses like cancer. This has now been replaced by a 'severity modifier,' which we, alongside others in the cancer community, do not believe appropriately recognises the severity of this advanced cancer.

Trastuzumab deruxtecan is the first breast cancer treatment that would have been eligible for the previous end-of-life criteria assessed under the new NICE methods; and now sadly becomes the first such breast cancer treatment to not be recommended by NICE in many years.

For the avoidance of doubt, we recognise that NICE does a very important job ensuring that new medicines are recommended for routine use if they represent a cost-effective use of NHS resources. It is important to emphasise that since NICE was established in 1999, the policy approach to reimbursing medicines in England has been conducted on the basis of the additional value new medicines offer to the NHS compared to current standards of care, not affordability or price per se.

As you know, the way NICE determines value is via a process of cost-effectiveness analysis, which considers a large range of complex factors to determine if the clinical and cost impacts of a new medicine provide value-for-money compared with current standards of NHS care. In simple terms, NICE determines the incremental health benefits - via a measure called a Quality Adjusted Life Year (QALY) – and the incremental costs compared to existing clinical practice, and works out whether the financial 'cost per QALY' falls within a cost-effectiveness threshold range.

NICE's standard threshold is between £20,000–£30,000 cost per QALY. This threshold has not changed since it was introduced at the same time NICE was established in 1999. By contrast, the Treasury Green Book valuation of a QALY is £70,000 per QALY by 2021/22 prices.[1] This is vital context, as it essentially means the threshold of allowable value has not risen with inflation in the same way that we would expect for all other aspects of public spending. Put another way, public policy in England continues to devalue in real terms year-on-year the extra years of life that new medicines can offer to patients.

In this broader context, NICE's new formula now quantifies the severity of a disease and applies either the standard threshold (x1 modifier), medium severity (x1.2 modifier), or high severity (x1.7 modifier), the latter of which is commensurate with the previous end-of-life weighting. The removal of the end-of-life criteria and the introduction of the severity modifier has resulted in metastatic HER2-low breast cancer in effect being defined as a disease with only 'medium' severity, achieving a lower x1.2 modifier making it much more difficult to demonstrate cost-effectiveness.

The trial population for this use of trastuzumab deruxtecan involved women who were on average 56 years old, with under 18 months left to live with standard chemotherapy treatment.[2] As highlighted in our submission to NICE, this medicine extends survival by an average of 7 more months. Quite understandably patients with such a prognosis and clinicians do not believe this to be a 'medium' severity disease - as highlighted by the unprecedented public response both to the appraisal consultation and subsequent petition initiated by Breast Cancer Now.

After careful consideration, we have taken the decision not to appeal the NICE decision. Our rationale is that the appeal process only allows us to contest where NICE policy has been misapplied, and though we disagree with the policy, it has been applied as is written. Therefore, an appeal on such grounds would be destined to fail. Instead, it is the policy itself which needs to change.

The inequity of patient access in the UK could not be any more stark. This medicine is already reimbursed in other types of breast cancer across the UK. It was reimbursed for this specific patient population in Scotland in December 2023. It is notable that the SMC retained the use of its end-of-life criteria in their assessment of this and other cancer medicines.

England, and thereby Wales and Northern Ireland (which adopt NICE's recommendations), stand increasingly isolated in its approach to assessing this treatment and other similar cancer innovations on the near horizon. This is illustrated by the 15 other countries in addition to Scotland including Canada, Germany, Italy, Bulgaria, Slovenia and Sweden that have already reimbursed trastuzumab deruxtecan for use in HER2-low metastatic breast cancer.

Access for these patients in England, Wales and Northern Ireland need not be delayed by lengthy or complex reforms. An immediate solution to the inequity facing HER2-low patients would be to extend the qualification criteria of the severity modifier. NICE's own analysis has found that the severity modifier is being underutilised since introduction in 2022, as does evidence from the ABPI. In NICE's board meeting 20th March 2024 they acknowledged "lower than expected use of the severity modifier" and that they would conduct a review this year of its implementation.[3] The warning signs are already there that this policy is failing these patients. We urge the acceleration of that review, and flexibility while these implementation problems are explored.

We would suggest an immediate interim pragmatic solution which would not require fundamental reform to implement. We propose modulating the proportional shortfall threshold for the high severity (x1.7) modifier from 0.95 to 0.90 (in simpler terms, changing the categorisation of a disease from having taken 95% of a person's quality adjusted life years to 90% of them). This would bring the high severity category back into broad equivalence with the previous end-of-life criteria, at least until a comprehensive review of the severity modifier has been completed. NICE have recognised their new methods are in an implementation phase, and our proposal here would add flexibility during this period so that advanced cancer patients are not disproportionately impacted.

With the recently signed 2024 Voluntary Scheme for Branded Medicines Pricing, Access and Growth (VPAG), there is now more headroom for funding innovative medicines due to an increase in the capped scheme spending.

Daiichi Sankyo and AstraZeneca remain committed to creating sustainable and equitable access for these patients in England, Wales and Northern Ireland, as well as finding a way forward for future advanced cancer patients who will be impacted by the recent formula changes – one that appropriately recognises the severity of this disease and the value of the medicines that target it.

Yours sincerely,

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References

[1] HM Treasury. 2022. The Green Book | Central Government Guidance on Appraisal and Evaluation| Available at: https://assets.publishing.service.gov.uk/media/623d99f5e90e075f14254676/Green_Book_2022.pdf

[2] Modi S et al. NEJM. 2022;387(1):9-20.

[3] NICE Public Board Meeting, 20 March 2024. Available at: Public board meetings | Board | Who we are | About | NICE