SETTING THE BAR TOO HIGH:

HOW THE NICE SEVERITY MODIFIER IS BLOCKING ACCESS TO LIFE-EXTENDING TREATMENTS

BREAST CANCER NOW
The research & support charity

FOREWORD

I was diagnosed with breast cancer in 2012 at the age of 29. A decade later, in July 2022, I found out the cancer had spread to my bones and was now incurable. The week this report is launched marks 3 years with a disease most people don't survive beyond 5 years.

Fortunately, thanks to incredible drugs and surgery, I'm currently classed as 'no evidence of active disease' – the closest thing to 'cancer-free' I will ever hear.

I'm an author, a journalist, a broadcaster and a campaigner. I'm a daughter, a wife, a sister, a friend, an aunty and a stepmum. And at 42, I'm alive thanks to drugs approved by NICE and provided on the NHS.

But cancer is clever. My cancer is currently sleeping, but it will wake up. It may take years, but my cancer will become resistant to the drugs. I'll work my way through new lines of treatment, but when those run out, I will die, leaving my parents heartbroken, my husband without the wife he needs by his side.

In the 13 years I've lived since diagnosis, I've written a book, got married, seen my beautiful nieces and stepdaughters grow. I've contributed so much to society, helping people through my writing and podcasts.

Breast Cancer Now's report shows with devastating clarity that the current system is not fit for purpose. It's letting down the people who need it most. It's denying us precious months or years of life.

If NICE doesn't change its severity modifier, there's a real risk I will be denied drugs that could make the difference of me seeing my stepdaughters and nieces go to university and get married. It could make the difference of me burying my parents or my parents burying me.

We must urge NICE to change its severity modifier, not just for Enhertu now but for all the drugs we will need to stay alive in future. Quite simply, secondary breast cancer is not a medium-severity disease – it's a disease that can kill within months, a disease that robs children of their mothers and parents of their children.

We're counting on those who have the power to make this change.

Thank you
Laura Price

SUMMARY

What's the problem?

- The National Institute for Health and Care Excellence (NICE) makes decisions about which drugs can be made available on the NHS in England by looking at how much life – and the quality of that life – a treatment will give someone. They will pay a set amount of money for each 'quality adjusted life year' (QALY) a new treatment offers. Wales and Northern Ireland usually adopt their decisions.
- There is some flexibility in their calculations to account for the fact that the public is willing to spend more on drugs in certain circumstances. Until 2022, they offered this flexibility through the 'end-of-life modifier', which allowed the NHS to spend more on drugs used to treat people in the last 2 years of their life.
- While this led to lots of drugs for advanced cancers being approved, it meant people with other serious conditions could miss out on treatments.
- So, in 2022, NICE changed to the 'severity modifier', which instead allows the NHS to spend more on treatments for more severe conditions.

What's the impact?

- NICE has set thresholds for what counts as moderately severe and very severe, and how much the NHS can spend on drugs for these conditions. This has led to drugs for serious conditions like cystic fibrosis being approved.

- **But it's meant that many drugs that would previously have got the end-of-life modifier don't qualify as very severe and the NHS can't spend as much on them as before. In short, it's meant some cancer drugs not getting the same priority as before.**

- Lots of drugs have still been made available thanks to negotiations with drug companies, but we've already seen some, such as Enhertu, be rejected. And we don't think it'll be the last.

- We also have strong reason to suspect that some drugs aren't being put through the full assessment process because the drug companies know they won't be approved, in part because of the severity modifier.

- **The upshot of this is some people with less than 2 years to live are being given the message that their condition is not severe enough for them to get the drugs they need to stay alive.**

What needs to change?

- NICE set the bars for what counts as severe to prevent an increase in the amount of money the NHS spends on drugs. They didn't have any solid evidence for their thresholds. And despite promising to do so, they also didn't commission any research to fill these evidence gaps for another 2 years.

- We think the bars need lowering. And both public opinion and international comparisons back this up.

- That's why we're calling on the Department of Health and Social Care (DHSC) to remove the restraints that are holding them back, and NICE to lower the bar for severity so that people with months left to live can get the drugs they need to stay alive.

- And we're calling on them to do it urgently, because people with incurable secondary breast cancer don't have time to wait.

"How can a disease that kills 31 women a day not be classed as very severe? How can this disease be considered moderate?"

- Alison, living with secondary breast cancer

INTRODUCTION

Secondary, or metastatic, breast cancer occurs when breast cancer spreads to other parts of the body. While there are treatments that aim to slow down its progression and give people more time, secondary breast cancer can't be cured. That means people with this devastating disease rely on having access to the drugs they need to keep them alive.

We have a bold vision – that by 2050, everyone diagnosed with breast cancer will live, and be supported to live well. But getting there will depend on people getting access to the best possible treatments.

People affected by the disease tell us that access to new treatments is one of their biggest priorities. And this is also a priority for government. The Health Secretary, Wes Streeting, has talked about making the UK a powerhouse for life sciences. And the call for evidence on the national cancer plan for England commits the NHS to ensuring that patients have access to the latest treatments, digital tools and technologies[1]. Because developing new and effective treatments isn't enough – we need to make sure that they're available to the people who can benefit from them.

Over the last 10 years, many new drugs for secondary breast cancer have been approved for use across the UK. These have transformed lives, allowing people to live longer in better health, giving them more moments with family and friends and doing what matters to them. But right now, we think this progress is at risk.

Because of the way drugs are now being assessed, some life-extending treatments for secondary breast cancer won't be available. That means thousands of people every year could be denied the drugs that can keep them alive. We've already seen Enhertu for HER2-low secondary breast cancer rejected by NICE. And we don't think it will be the last.

We think that the mechanism for approving drugs is the problem. In particular, the severity modifier. We think NICE has set the bar too high. And it's been set without proper evidence to back it up. We're in a situation where people who have a matter of months left to live can be denied the drugs they need to keep them alive, because their condition isn't considered severe enough.

We're calling for the system to change. The bar for severe conditions needs to be lowered, and it needs to be done now. Because people with secondary breast cancer don't have time to wait.

ACCESS TO MEDICINES IN THE UK

The drug approval process

In England, the organisation that decides whether drugs can be made available on the NHS is the National Institute for Health and Care Excellence, usually known as NICE. They make recommendations that apply in England, but these decisions are also usually adopted by Wales[2] and Northern Ireland[3]. Scotland makes their own decisions through their equivalent of NICE, the Scottish Medicines Consortium (SMC).

NICE makes its decisions about whether to recommend a new drug after looking at all the available evidence. This includes how effective it is and how much it will cost the NHS – altogether, its 'cost-effectiveness'. This process is called a health technology assessment, or HTA.

EXAMPLE DRUG

Anne is 65 and living with an advanced cancer. She has been told by her doctors that she has limited treatment options and is likely to die within the next 2 years.

Generitax is an exciting new treatment for Anne's cancer. It's been shown to be safe and effective in clinical trials. It could mean she will live 6 months longer than she would on standard treatment. Anne has young grandchildren and is desperate to access the drug so that she can spend more time with them as they grow up.

Generitax has been submitted to NICE for a health technology assessment to see if it can be offered on the NHS.

Quality-adjusted life years (QALYs)

To make decisions on the cost-effectiveness of a new drug, NICE uses the health economics concept of the 'QALY' or quality-adjusted life year. This takes into account the number of years a treatment could be expected to add to a person's life, as well as the quality of that life.

The preferred measurement for quality of life is the EQ-5D[4] – a way of measuring quality of life based on a person's own assessment of it. The EQ-5D takes into account how someone rates their mobility, ability to do their usual activities and look after themselves, and their levels of pain, discomfort, anxiety and depression. Quality of life is measured on a scale of 1 to 0, where 1 is perfect health and 0 is death.

How do NICE calculate cost-effectiveness?

NICE work out how many QALYs the drug could give to patients by multiplying the amount of extra life a drug could give (in years) and the quality of that life (on a scale between 0 and 1).

EXAMPLE DRUG

Generitax is expected to offer people like Anne an extra 6 months of life (0.5 years). Her cancer has some symptoms and the treatment has some side-effects, so the quality of that life is rated as 0.6. The number of years (0.5) is multiplied by the quality of life (0.6), to give the number of additional QALYs the treatment could offer. For **generitax**, this is 0.3 QALYs.

They'll then consider how much it costs. This includes both the cost of the drug itself and all the costs to the NHS of introducing the medicine.

EXAMPLE DRUG

Generitax has a 'list price' of £2,000 per pack of tablets. It is being offered to the NHS with a discount but this is kept confidential. Because it's a tablet, Anne wouldn't need to come into hospital for her treatment, which suits her. But she'll still need regular monitoring of her bloods and extra scans while being treated to pick up on any serious side-effects. All these costs are added up.

Finally, they'll also look at how certain they are of the effectiveness and cost data. The figures on both the costs and benefits of the treatment will be estimates, so they'll consider how sure they can be that the figures are accurate. This process allows them to work out the price per QALY of the new medicine.

How much will they spend?

The NHS sets a standard amount of money they'll pay for each additional QALY a treatment offers. This 'cost-effectiveness threshold' is £20,000-30,000 per QALY. This figure hasn't been adjusted for inflation in more than 20 years – a point we'll return to later.

- If the medicine comes in below this threshold, NICE can recommend it for use in the NHS in England. Wales and Northern Ireland usually follow suit.
- If the medicine comes in above the threshold, the drug company and NHS England may try to negotiate a new price. But if that isn't possible, the drug will be rejected and patients won't be able to access it on the NHS.
- If there's a high level of uncertainty around its cost effectiveness, NICE might recommend that it's made available temporarily, such as through the Cancer Drugs Fund. They'll then wait for more evidence, so they can make a longer-term decision.

EXAMPLE DRUG

Generitax is an expensive drug, despite the confidential discount. Its total cost to the NHS comes in at £45,000 per QALY, far above the £20,000-30,000 cost-effectiveness threshold. Unless a special deal on price can be done with the company, NICE will reject the drug and Anne won't be able to access it on the NHS.

THE SEVERITY MODIFIER

Using such a technical process to decide who gets which treatments can feel dehumanising. Particularly when we think about emotive topics like access to life-extending drugs for people with life-limiting illnesses.

NICE does try to reflect public opinion in the way they make their decisions. And because of this, they accept that more flexibility is sometimes needed to bring about the right outcomes.

Their own review of the evidence showed that in certain circumstances, the public is willing to pay more than the standard £20,000-30,000 per QALY[5]. The way they account for this preference is through the use of modifiers.

The end-of-life modifier

Up until 2022, NICE accounted for this public preference through the 'end-of-life modifier'. This was an additional weighting that allowed them to pay more for treatments used to treat people in the last 2 years of their lives. For these treatments, they could pay up to £50,000 per QALY – nearly 1.7 times the standard amount.

The end-of-life modifier allowed NICE to approve lots more treatments for advanced cancers. These included trastuzumab emtansine (Kadcyla) for HER2-positive secondary breast cancer[6] and alpelisib (Piqray) with fulvestrant for some HR-positive, HER2-negative secondary breast cancers[7].

EXAMPLE DRUG

Generitax is targeted at patients like Anne with an average of 18 months left to live and it can give them, on average, an extra 6-months. Under the old system, this means it qualifies for the end-of-life modifier and gets a cost-effectiveness threshold of up to £50,000 per QALY. With a cost to the NHS of £45,000 per QALY, this means it can be approved and Anne would be able to access it.

But in 2022, NICE retired the end-of-life modifier and introduced the 'severity modifier' in its place, which bases decisions on how severe the condition being treated is.

The severity modifier

In simple terms, the severity modifier means that the more severe a condition is, the more weighting it gets, and the more the NHS will spend on drugs to treat it.

The modifier works as a multiplier. So, severe conditions get a multiplier based on whether they are considered moderately or very severe, which raises the cost-effectiveness threshold. For very severe conditions, the NHS can spend up to £51,000 per QALY.

But severity is not an easy thing to measure objectively. Some conditions can have a bigger impact on people's quality of life, or on their ability to do certain things. While other conditions can take away more years of a person's life. Comparing these different types of severity is complicated.

NICE measures severity by looking at 2 concepts – absolute QALY shortfall (AQS) and proportional QALY shortfall (PQS). These are supposed to be objective measures of how much of a person's life – and the quality of that life – a condition will take away.

Absolute QALY shortfall and proportional QALY shortfall

Absolute QALY shortfall, or AQS, measures the actual length of life – and the quality of that life – that people lose as a result of their condition.

It's calculated by taking the total QALYs that similar people without the condition would be expected to have over the rest of their lives, then subtracting the QALYs people with the condition would be expected to have with the currently available treatment.

EXAMPLE DRUG

Anne's cancer has an average life expectancy of 18 months (1.5 years) at a quality of life rated as 0.6, which translates to 0.9 QALYs. NICE expects that someone like Anne without the condition would live around another 17 years at a quality of life rated 0.8, which translates to 13.6 QALYs.

The QALYs with the condition (0.9) are subtracted from QALYs without the condition (13.6) to give an AQS of 12.7.

Proportional QALY shortfall, or PQS, measures the proportion of life – and the quality of that life – lost by people living with a condition. It's calculated by taking the AQS and dividing it by the QALYs that similar people without the condition would be expected to have. Here, we've shown this as a percentage.

EXAMPLE DRUG

Anne's cancer has an AQS of 12.7, whereas someone without the condition would be expected to have a total of 13.6 QALYs. So the PQS is 12.7 divided by 13.6, which gives a PQS of 93%. In short, that means Anne is losing 93% of the life – and quality of life – that she could expect if she didn't have the condition.

THE SEVERITY THRESHOLDS

NICE has set thresholds that the AQS and PQS figures need to reach for a condition to be considered severe. In short, these are bars that conditions have to clear for NICE to be able to spend more money on drugs for them.

Very severe

AQS* OF AT LEAST 18, OR PQS* OF AT LEAST 95%	→ THE CONDITION GETS THE HIGHEST SEVERITY MODIFIER OF 1.7	→ THE COST-EFFECTIVENESS THRESHOLD GOES UP TO THE MAXIMUM £51,000 PER QALY*

Moderately severe

AQS* BETWEEN 12 AND 18 OR PQS* BETWEEN 85% AND 95%	→ THE CONDITION GETS A LOWER SEVERITY MODIFIER OF 1.2	→ THE COST-EFFECTIVENESS THRESHOLD ONLY GOES UP TO £36,000 PER QALY*

Not severe

AQS* BELOW 12 AND PQS* LESS THAN 95%	→ THE CONDITION ISN'T CONSIDERED SEVERE AND DOESN'T GET A MODIFIER	→ THE NORMAL £20,000 -30,000 PER QALY* THRESHOLD APPLIES

"A disease with a life expectancy of 3-5 years is not moderate. Once a treatment stops working it can kill us within months."

- Viv, living with secondary breast cancer

*Quality-adjusted life year (QALY), Absolute QALY shortfall (AQS), Proportional QALY shortfall (PQS).

EXAMPLE DRUG

For Anne's cancer, the AQS is 12.7 and the PQS is 93%. This means her condition is only considered moderately severe.

NICE will apply the lower severity modifier, giving a cost-effectiveness threshold of £36,000 per QALY for the treatment. But since **generitax** costs £45,000 per QALY, unless a very generous deal is reached with the company, it can't be approved.

So, while Anne's condition has a short life expectancy, she won't be able to get the drugs she needs.

If **generitax** had qualified for the highest severity modifier, the cost-effectiveness threshold would have been £51,000 per QALY and it would have been approved, allowing Anne to get access to the treatment.

Why did NICE change to the severity modifier?

In the early 2020s, many people felt that the end-of-life modifier wasn't working for everyone, and we agreed. It was being used exclusively on cancer treatments and didn't take into account that the public might want to pay more for treatments for other very serious conditions as well.

As it was, drugs for these conditions weren't qualifying for the end-of-life modifier and so people were less likely to be able to get them.

In 2020 and 2021, NICE carried out a large-scale review of their methods and processes. One thing they looked at was 'decision modifiers' like the end-of-life modifier. They looked at all the existing literature on the public's preferences on decision modifiers. And they engaged with stakeholders, including with patient organisations and charities. But they didn't do any primary research, either quantitative or qualitative, with the general public.

Their review did find evidence that the UK public supports giving special consideration to end-of-life conditions. However, they found a lack of consensus on whether this should be applied in the context of treatments that increase life expectancy, improve quality of life or both.

They also found evidence that there is support for a modifier focused on the 'burden of illness'. This is what became the severity modifier. They also noted that there was 'some correlation between end of life and burden of illness'[8].

The final report on decision modifiers proposed 'moving beyond' the end-of-life modifier to instead favour treatments for people with more severe diseases. NICE's analysis at the time showed that this would have a negative impact on new treatments that would previously have got the end-of-life modifier. Of the 65 treatments that had been approved with the end-of-life modifier, 44 would receive a reduced severity modifier and 7 would receive no modifier at all[9].


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NICE, NHS ENGLAND,
DAIICHI SANKYO, ASTRAZENECA:
GIVE US TIME TO LIVE
MAKE LIFE-EXTENDING DRUG ENHERTU AVAILABLE ON THE NHS NOW!
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THE IMPACT OF THE CHANGE

NICE has said they're committed to monitoring the severity modifier. They published their first review of its implementation in September 2024[10], which found that the modifier was 'operating as intended'. This was based on the fact that it had remained broadly 'opportunity-cost neutral' – a concept we'll return to later – and had been applied to a wider range of conditions.

But if we dig a bit further into the data, we find some worrying outcomes.

Cost-effectiveness thresholds

Under the new system, 21 treatments that would previously have qualified for the end-of-life modifier also got a severity modifier. But only 7 of these were judged to be for very severe conditions, meaning they got a cost-effectiveness threshold of £51,000, similar to what they would have got under the old system.

The other 14 were only found to be for moderately severe conditions and had their cost-effectiveness threshold cut to £36,000. That's a full £15,000 per QALY lower, around 30%. This is a clear disadvantage compared with the previous system.

Approvals and rejections

NICE has also said that the severity modifier has not led to a major drop in approvals for advanced cancer medicines. And in some ways, they're correct. In many cases it seems that this is because drug companies have been willing to make deals to make their medicines available. But for some advanced cancer drugs, it has caused insurmountable issues.

Enhertu[11]

Probably the clearest example of this happening is Enhertu (trastuzumab deruxtecan) when used to treat HER2-low secondary breast cancer. This is the first licensed targeted treatment for HER2-low secondary breast cancer and could give around 1,000 people a year in England (and more in Wales and Northern Ireland) an extra 6 months of life, on average. We think it would have qualified for the end-of-life modifier.

Enhertu was approved in Scotland for these patients in late 2023 and is available in more than 20 other European countries. The cost has not caused insurmountable issues elsewhere. But Enhertu was rejected by NICE for use on the NHS in England in 2024, following an appraisal where the condition was judged to only be moderately severe. That meant it only got a 1.2x severity modifier.

Despite seeking an appeal, gathering the signatures of 300,000 people, engaging with all parties and involving the Secretary of State for Health, we haven't been able to overturn this deeply troubling decision and people are still unable to access this treatment in England, Wales and Northern Ireland.

IsaPD[12]

Isatuximab, pomalidomide and dexamethasone (known as IsaPD) is a combination treatment for people with relapsed and refractory multiple myeloma. It's been shown to improve remission times by more than 12 months.

When NICE considered it in 2020, they applied the end-of-life modifier and it was approved for use on the Cancer Drugs Fund as an interim arrangement. Since then, around 1,500 people have benefited from the drug, and it was also made available in Scotland in 2021.

However, in 2024 when NICE went to review the guidance to decide whether IsaPD would be made available permanently, they used the new severity modifier. They found it no longer met the cost-effectiveness threshold to be made available through the NHS[13].

The company involved, Sanofi, and patient charity Myeloma UK both successfully appealed this decision on grounds of fairness. As a result, IsaPD remains available for now. However, NICE will need to reconvene to address the findings of the appeal and make a new decision[14].

What the NICE data doesn't show

NICE figures on rejections also don't tell us the whole story.

The process of going through a health technology assessment is expensive for drug companies.

The costs vary depending on the size of company, but for large companies, who produce most oncology drugs, the cost for a single appraisal in 2025/26 is £186,100[15]. And when you take into account the amount of work needed to prepare a submission, the cost gets significantly higher.

While drug companies may be able to afford this, it stands to reason that if their own calculations show that a medicine is unlikely to be approved at a price they're willing to offer, they'll choose not to go through this process. A recent report from the Blood Cancer Alliance[16] found that of the 210 oncology appraisals started by NICE in the last 5 years, 23% were terminated, meaning they were stopped before they reached a recommendation.

Drug companies don't tend to give very specific reasons for terminating applications, and they may happen for a number of reasons. These include poor clinical trial data or issues with licensing. But a large proportion will be because of issues with the UK drugs market that make it harder for drugs to be approved here at a competitive price.

The Blood Cancer Alliance's report looked at the published reasons behind these terminations and found that the most common reason for termination was the submission being 'unlikely to achieve cost-effectiveness'.

Terminated appraisals don't tend to attract the same public attention and campaigning activity as NICE rejections, but their impact is the same – people who desperately need to access drugs are unable to get hold of them.

Delayed and terminated appraisals

- Sacituzumab govitecan (Trodelvy) is a treatment we campaigned hard for people with triple negative secondary breast cancer to be able to access. It's already licensed in the UK for people with HR-positive, HER2 negative secondary breast cancer, meaning it's been passed as safe and effective. And it's been approved for use in 18 countries, including France, Canada and Sweden. The NICE appraisal began in 2022, but it is currently stalled[17], with the company unable to offer any information about when it might proceed.

- Enhertu is licensed for use in HER2-mutant non-small cell lung cancer and HER2-positive stomach cancer. But it remains unavailable for these patients, because the NICE appraisals have been terminated[18].

- In other parts of the world, Enhertu is being considered for use in HR-positive, HER2-low secondary breast cancer, based on findings of the Destiny Breast 06 trial. Again, the appraisal for this use of Enhertu in England has been suspended[19], so these patients will be unable to access the treatment in England, Wales and Northern Ireland.

- Enhertu is currently available through the Cancer Drugs Fund for 2 HER2-positive secondary breast cancer indications, one of which qualified for the end-of-life modifier. But the future of these uses is uncertain as the decision on whether it will enter routine commissioning will be made under the severity modifier.

We don't think these delays and terminations are entirely because of the severity modifier. Companies face multiple challenges in the UK market. These include:

- High rebate costs through the VPAG scheme (the voluntary scheme for branded medicines pricing, access and growth, an agreement between DHSC, NHS England and the pharmaceutical industry body the ABPI) – companies agree to pay back any money the NHS spends on drugs above a certain level through rebates. This limits their ability to profit in the UK market.

- Inflexible approaches to things like indication-based pricing, which allows companies to charge different prices for the same medicine depending on the group of patients it is being used for and the outcomes it achieves for them. The use of this is currently limited in the NHS.

- Difficulty in reaching a cost-effective price for combination treatments (where 2 or more treatments are used together), especially when one or more of the drugs used in combination has already been approved as a single treatment.

But the severity modifier is an additional pressure. And it can tip some drugs over the edge, making them either likely to be rejected by NICE, or unlikely to even be put through a NICE appraisal.

We think that the full scale of this issue remains to be seen. In recent years we've seen concerning signs that the less generous system in England, Wales and Northern Ireland means we're falling behind the rest of the world in access to cutting edge cancer medicines. Yet this is not being picked up or reported on in NICE's reports on the severity modifier.

WHAT WENT WRONG?

The evidence base

While the evidence NICE looked at did show that the public has a preference for giving special consideration to severe conditions, it didn't capture the size of this preference. In other words, how differently they should be treated to other conditions.

This means the decisions NICE took about where they set the bar for what counts as moderately and very severe, and how much more the NHS could pay for these drugs, weren't based on evidence.

At the time, NICE acknowledged this gap. They said they'd set some initial thresholds without this evidence 'in order to avoid delay'[20]. These were presented to stakeholders as a stop-gap measure while more research was carried out. However, between 2022 and 2024, they failed to conduct or even commission any research to fill this gap.

But while they were slow to progress their research, others have attempted to fill the gap. A report by the Office of Health Economics[21] published in 2024 found that members of the UK public judged a 'severe health state' to start at around 50% PQS (compared to NICE's 85%) and that very severe health states begin at around 65% (compared to NICE's 95%).

This is only one study, and it was funded by the Association of the British Pharmaceutical Industry (ABPI). But its findings are so radically different to the current, unevidenced thresholds that we have to ask how appropriate the current thresholds are.

Opportunity-cost neutrality

Under the old system, the NHS was allowed to spend nearly 1.7x the standard amount per QALY on end-of-life conditions. But the government didn't want to add more additional 'weighting' into the new system, as this might have led to them spending more money on drugs.

So, the amount of additional weighting available to severe conditions remained the same as under the end-of-life modifier. But it was spread more broadly to other non-cancer conditions. In simple terms, the pie remained the same size, but there were more conditions eligible to take a piece of it.

This meant that the bar for what counts as very severe – in terms of AQS and PQS – was set without evidence, and with the sole aim of making sure the new model remained 'opportunity-cost neutral' and didn't add more additional weighting into the system.

When coupled with the OHE report, it seems clear to us that NICE have set the bar for severity too high. It doesn't match what the public thinks counts as a very severe condition. It was done primarily to keep budgets from going up. And it puts us in the position where some conditions aren't considered very severe despite people having less than 2 years left to live.

How do we compare to other countries?

It can be difficult to compare and contrast health technology assessment criteria in different countries. But it's clear that other similar countries are more generous in how they allocate additional weighting to more severe conditions.

In the Netherlands, the health assessment body uses PQS in order to adjust cost-effectiveness thresholds[22]. The lowest severity conditions, with a shortfall less than 40%, only qualify for a 20,000 Euro (£17,000) threshold. But the most severe conditions, with a shortfall above 70%, could get a threshold of up to 80,000 Euro (£69,000), a full 4x higher. This 70% threshold is dramatically lower than the proportional QALY shortfall of 85% needed to get any modifier in the UK – let alone the 95% required to get the full 1.7x adjustment.

In Norway, a white paper proposed adjusting the acceptable cost-effectiveness threshold based on AQS[23]. The acceptable cost per QALY threshold would increase from 275 000 to 825 000 Norwegian Kroner (approximately £25,000 to £75,000) between the least severe and most severe conditions.

Sweden takes a more qualitative approach. They apply a greater cost-effectiveness threshold for conditions judged to be more severe, but these judgements are made by an assessment board on a case-by-case basis[24]. A review of Swedish HTA decisions up to 2019 suggests that they have applied an effective acceptable threshold of up to 1 million SEK (£90,000) per QALY gained for the most severe conditions, 750 000 SEK (£68,000) for severe conditions, and 500 000 SEK (£45,000) for moderate conditions.

"I have 3 little girls. My biggest fear is not being there to support them and see them grow. The thought of them living in a world where I no longer exist is excruciating. Let me have more options, more chance to see my little girls grow up. Let them have their Mummy a bit longer."

- Helen, living with secondary breast cancer

WHAT NEEDS TO CHANGE

We think immediate action needs to be taken. If it isn't, we risk further harm to the approval of end-of-life drugs and the people who so desperately need access to them.

We're calling on DHSC and NICE to act with urgency. To ensure that patients are able to access treatments. And to allow the government to deliver on its ambitions for the cancer plan and life sciences. Here's what we think they need to do.

Remove opportunity-cost neutrality

DHSC needs to remove the requirement for opportunity-cost neutrality in how the severity modifier is applied. This is at the root of the issues with the modifier. It pits end-of-life cancer treatments against other severe conditions like cystic fibrosis in a way that's reductive and unfair to patients. And, ultimately, it creates barriers to the approval of drugs for advanced cancers.

We need to increase the amount of additional weighting available for treatments for more severe conditions across the board, rather than just shifting the same amount of weighting around. In short, we need to increase the size of the pie. Otherwise, we simply get more diluted results for more conditions.

NICE has been clear that any change to the severity modifier that moves beyond opportunity-cost neutrality would need to be signed off by DHSC. We call on them to do this urgently.

Lower the bar for severity

Once the need for opportunity-cost neutrality is removed, NICE should lower the thresholds at which the modifiers are applied. This will bring the system more in line with other similar countries and the evidence on public preferences.

This also shouldn't be hard to do. It won't need a whole new methods review. They can do it through a modular update to their methods and processes.

NICE must not wait for their own societal preferences research to finish – this work has taken too long already, in large part because they didn't commission research when they had promised to. In the meantime, patients will continue to miss out on life-extending treatments, which is unacceptable. Given the nature of the conditions these people have, they don't have time to wait.

EXAMPLE DRUG

If the PQS threshold for a very severe condition was dropped from 95% to 90%, generitax could get the full £51,000 per QALY cost-effectiveness threshold. It could then be approved by NICE and Anne would be able to access it.

Longer term reforms

In the longer term, NICE should also carry out a review into other potential reforms to the severity modifier.

Make the severity modifier continuous

The severity modifier currently puts conditions into discrete and arbitrary categories of severity – not severe (1x), moderately severe (1.2x) and very severe (1.7x). Some conditions can narrowly miss out on a higher category of severity, but still be more severe than other conditions within their bracket – something the current system can't account for.

It makes more sense to consider severity as a spectrum. Redesigning the severity modifier to be continuous – where the multiplier moves up in line with the degree of severity – would be a better reflection of reality. This shouldn't add much additional complexity to NICE's calculations.

EXAMPLE DRUG

Anne's cancer has a PQS of 93%, placing it below the threshold for a very severe condition. Under a severity modifier with continuity between 1.2x and 1.7x, Anne's cancer could qualify for a 1.41x severity modifier, allowing **generitax** a price of £42,300 per QALY gained. This is less than its cost per QALY, but it is closer than before, and may make it easier to agree a special deal on price.

Change the multipliers

The current 1.2x and 1.7x modifiers are arbitrary. There's an argument that the most severe conditions shouldn't be constrained by the 1.7x modifier and a £51,000 per QALY cost-effectiveness threshold. By international standards, this is still low.

NICE should explore whether the highest multiplier should be increased to 2x or even beyond so that people with very severe conditions can get the medicines they need.

EXAMPLE DRUG

Being considered under a severity modifier with continuity between 1x and 2x would mean Anne's cancer qualified for a 1.59x severity modifier. This would give a cost-effective threshold of £47,700, which means **generitax** would be affordable for the NHS.

Review the £20-30,000 threshold

The cost of a QALY that NICE uses has not been adjusted for inflation in more than 20 years. The treasury green book currently values a QALY at £60,000, meaning that in other areas of government decision making, a QALY is valued much more highly. It seems strange that when it comes to life-extending drugs for severe illnesses, this extra life is valued much lower.

The £20,000-30,000 value is currently locked in as part of the commercial agreements between government and pharmaceutical companies (VPAG). But there are clear arguments that it should be raised in line with inflation when this agreement is next up for negotiation.

The role of drug companies

It's important to draw attention to the role of drug companies in making sure people can get the treatments they need. They have a responsibility to do everything they can to make sure their products are reaching patients.

Competitive pricing and flexibility in negotiations

Drug companies should set fair prices and do what they can to come to agreements that allow people to get the drugs they need.

EXAMPLE DRUG

If the pharmaceutical company that manufactures generitax were willing to significantly drop the price they charge for the drug, by around £9,000 per QALY, it's possible that it could be approved under existing thresholds.

Transparency and openness about challenges

Drug companies need to be open and transparent about the challenges they face in the drug appraisals process. Without this, it will be hard to tackle the issues and improve the process.

Negotiations around medicines usually happen under commercial confidentiality rules. This means patient groups and the public are often left in the dark about what's really going on. Companies should be as open as possible about what happens in these discussions.

And this transparency also applies to decisions to delay or terminate appraisals. This will help patients and the public understand what's driving these decisions. Companies mustn't use terminations as a tactic to avoid negative attention on decisions that will stop patients from accessing medicines that they need.

"I'm scared that Enhertu won't be the last drug to be blocked by the new severity modifier and that I'll miss out on crucial life extending treatments.

I'm scared I'm going to die whilst my daughter is still so young, and I'm angry that women are dying now, sooner than they need to."

- Kathryn, living with secondary breast cancer

CONCLUSION

The current system has already failed people with secondary breast cancer and we're concerned this won't be the last time. The bar for severity has been set too high, with people who have months to live being told their condition isn't severe enough for them to get the drugs that'll keep them alive.

DHSC and NICE need to fix this. By removing the requirement for opportunity-cost neutrality that's limiting how much weighting can be applied. And then by lowering the bar for what counts as a severe condition.

There's evidence that the public supports this. It brings us into line with other comparable countries. And it's in line with the current government's stated ambitions for the health system and life sciences.

This needs to be done, and it needs to be done now. We stand ready to work with the government and NICE to make sure these changes are delivered, so people living with secondary breast cancer have more time to live.

NOTES

Our relationship with the pharmaceutical industry

As the UK's leading breast cancer charity, it's essential we engage with the key stakeholders that will help us achieve our vision. The pharmaceutical industry has an absolutely crucial role to play in achieving this.

All our work with the industry is governed by our pharmaceutical policy, which ensures that we maintain our independence when it comes to speaking out on what matters to breast cancer patients, irrespective of funding. We do not accept funding from pharmaceutical companies for our policy and campaigning work or use pharmaceutical donations to fund our policy and campaigns work, which includes our work on access to drugs.

Our access to drugs work is driven by the evidence and patient need. We retain full independence in our campaigning and influencing activity, regardless of whether the charity has received funding from pharmaceuticals in the past.

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