

More deliberation and less maths

Making reasonable decisions about access to orphan medicines in the UK

**A Cancer52 Briefing Paper
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Summary

Orphan medicines treat diseases that affect no more than 5 in 10,000 people in Europe. Ultra-orphan treat those diseases that are even more rare. Rarer cancers make up close to 40% of orphan medicines.

It's a difficult and long journey for an orphan medicine to reach the patient, and difficult decisions need to be made about the benefit and risks of orphan medicines when we can't always have the robust evidence that regulators and the NHS wants.

Orphan drugs can be assessed not just for their clinical benefits and risks, but also their value for money. Three main agencies do this across the UK using cost per Quality Adjusted Life Years (QALYs) calculations. But this approach doesn't capture everything that it should for orphan medicines. Partly in recognition of this, but also due to political pressure, changes are being made. These focus on considering more criteria (like absence of other treatment options) and more engagement with patients and carers: ***more deliberation and less maths*** should inform decisions to recommend or reject orphan medicines.

Cancer52 thinks changing the way that access is determined is a step in the right direction: that such decisions need to account for the special circumstances faced in treating rare diseases. And more decisions about smaller patient groups will be needed in the era of precision medicines.

But we might not need every agency to do that job.

Cancer52 is asking for:

- **Full and open approach to evaluation of changes.** This should include how far proposals/changes in appraisal affect research priorities, including research for those with rare and less common cancers. Cancer52 is willing to work with all stakeholders to build on the opportunities of reform and to improve access to medicines in the UK
- **A debate on the merits of a single UK wide approach to appraising ultra orphan medicines**
- **Faster decisions** from agencies – patients can't always wait the time it takes for recommendations to be made

Background

Orphan medicines are medicines that treat diseases that affect no more than 5 in 10,000 people across Europe as classified by the European Medicines Agency (EMA). Cancer52 are particularly interested in orphan medicines because close to 40% of currently approved orphan medicines are for use in rare cancers.¹ Orphan medicines are often further divided into those that are for very small populations (1 in 50,000 has been used) and known as 'ultra-orphans'. Everyone should be clear about which definition is being used and how their approaches to making decisions differ when a drug is for very very small populations, through to small populations.

A difficult and long journey to the patient

Cancer52 understands that the decision to take an orphan medicine is the culmination of decisions made by developers, manufacturers, regulators, and clinicians and patients themselves. That's because an orphan medicine will have had to be scrutinized not just for its safety, efficacy, effectiveness, commercial viability and for its suitability for a particular patient (just as for any medicine including those for more common conditions). But there are special features of orphan drugs:

- that the patient numbers are small, and sometimes very very small
- that exploring their benefits and risks is hard and may not provide robust safety, efficacy and effectiveness evidence
- that developing them can be costly with a small market, and their prices follow on from this

It is a difficult balance to decide when the risks are worth taking but for some patients, the benefits can be life changing.

Many agencies across the UK look at the value for money of orphan medicines

Increasingly orphan medicines are also subject to scrutiny of their value for money.

Across the UK, the main agencies include:

The Scottish Medicines Consortium (SMC)

The All Wales Medicine Strategy Group (AWMSG)

The National Institute for Health and Care Excellence (NICE)

Reasonable decisions need reasonable methods....

Agencies like NICE, and the others, use cost utility analysis (CUA) to explore the costs and benefits of orphan drugs. The 'utility' part is intended, in theory at least, to explore the benefit to patients. This is typically through the Quality Adjusted Life Year (QALY). But there has been concern for some time that the QALY model doesn't capture everything that's relevant for orphan medicines, and perhaps, is even less appropriate for ultra-orphans. Problems include whether measures that should pick up public preferences, utility of patients, and the carer perspective are really captured. This is even with some of the special criteria or 'modifiers' that some of these agencies might apply already.

...and reasonable processes.

¹ Based upon our review of Orphanet, Lists of medicinal products for rare diseases in Europe, January 2014
http://www.orpha.net/orphacom/cahiers/docs/GB/list_of_orphan_drugs_in_europe.pdf



Alongside concerns about the methods used, there has also been debate about the processes used, and the role of patients and carers in how these decisions are reached and how their evidence is able to inform the decision.

Together, these concerns about methods and processes, has resulted in too many 'no's' from NICE, SMC, AWMSG and not enough 'yeses'.

Positive changes in approaches to account for rarity, but no consensus across the UK

The agencies across the UK are all making changes to how they approach consideration of orphan drugs, summarized in Table 1. But the big change is simply that agencies realize that what they have been doing needs to change, and we believe that these changes must be for the benefit of patients.

Table 1: Summary of proposed/ongoing changes being made in how agencies approach appraisal of medicines

	NICE* (VBA from late 2014, first HST appraisal ongoing)	SMC (from April 2014)	AWMSG* (awaiting Government response to proposals)
Medicines for common diseases	- <u>Value Based Assessment (VBA)</u> which includes new criteria: Burden of Illness (BoI) and Wider Society Benefit/Impact (WSB/WSI)	- <u>Meetings in public</u>	
Orphan medicines		- Flexible definitions between orphan and ultra-orphan - Additional opportunities for patient interest groups (PIG) to input: <u>"a determining factor in decisions made"</u> - Introduction of Patient and Clinical Engagement (PACE) meeting	<u>Proposals</u> for - Multi-criteria approach with additional weights applied to QALYs - Greater involvement, including with patients and new Orphan/Ultra-orphan Medicine Group to provide advice to AWMSG - Not necessarily appraised by AWMSG but can be referred back if large number of Individual Patient Funding Request (IPFR)
Ultra-orphan medicines	- Testing of <u>NICE's proposals for Highly Specialised Technologies (HST)</u> : a multi-criteria approach without weighting and scoring – includes criteria such as available treatment options - Cost effectiveness remains part of the framework - Budget impact important and links to NHS England and their budget for specialised services and within that, for orphan and ultra-orphan medicines	- Multi-criteria approach without weighting and scoring - Cost effectiveness remains part of the framework	- As above
Medicines used at the end of life (EoL)	- Incorporated under VBA - Potentially upper limit of £50,000 per QALY - Replacement of EoL criteria – but 'uplift' should remain in some form	- Shared approach with orphan medicines - Disagree with NICE EoL criteria	- Additional weights applied to QALYs based on NICE EoL criteria

	NICE* (VBA from late 2014, first HST appraisal ongoing)	SMC (from April 2014)	AWMSG* (awaiting Government response to proposals)
Exceptionality**	- Managed separately to NICE on a central basis by NHS England - Where there appears to be a cohort of patients, then the drug is assessed for inclusion in a commissioning policy or requests can be made via an Individual Cancer Drugs Fund Request for Funding (ICDRE)	- Individual Patient Treatment Requests (IPTRs) will be funded from the Rare Disease Medicines Fund up to April - IPTRs will be replaced by the Peer Approved Clinical System (PACS) which will place greater emphasis on clinical opinion	- Managed separately to AWMSG on a regional basis by the Local Health Boards but if a large number of IPFRs, the drug can be referred back to AWMSG

* Not all medicines are subject to NICE and AWMSG appraisal **where an individual patients circumstances mean that they can be considered for funding on an individual basis – clinically driven approach to funding requests

What these amount to is a move away from the more rigid cost per QALY model, incorporating more criteria and greater engagement with patients and carers: more deliberation than maths should inform decisions to recommend or reject orphan medicines.

But these approaches must also respond to wider changes in the science: we know much more about genes and increasingly the role of mutations which can affect the efficacy and effectiveness of new medicines. This means that society will need to make more decisions about smaller and smaller patient groups: more drugs may well be 'orphans' in the future.

In Scotland, the changes are driven by a clear desire to increase access to orphan medicines (and those used at the end of life, which sometimes overlap): basically securing more 'yeses' from the SMC.

Other changes will undoubtedly come, including proposals for a 'Scottish Model of Value'.

Alongside these changes, new policies have also been pursued: in England there is a Cancer Drugs Fund (CDF) that sometimes pays for orphan medicines, and in Scotland a Rare Conditions Medicines Fund (RCMF). Up until April, this will pay for all Individual Patient Treatment Requests (IPTRs). Wales has not adopted such approaches.

The politics of orphan medicines

What all of this really boils down to is that it is hard, and politically fraught, to make decisions about expensive medicines that treat rare conditions. No single system in the UK has found a way through without criticism.

And when agencies have said no, politicians have been quick to add on other ways to achieve 'yeses' even if that isn't for all patients or all medicines: either by ring-fenced funding or directing changes to agencies to achieve this.

The development of country specific models of value seems to reflect a desire to demonstrate independence, as so far, little research has really explored whether the public and patients hold different views on the value of medicines for rare diseases within the UK.

What does Cancer52 think is reasonable?

Cancer52 doesn't think it's reasonable to leave those with rare conditions behind. And orphan medicines are part of the broader diagnosis, care and treatment that they deserve. But we know that the NHS can't pay for everything, that not all new medicines are really breakthroughs, and that difficult decisions have to be made. We want patients with rare cancers to be part of making those decisions: it is their lives that can hang in the balance.



Cancer52 does think it's reasonable to use methods and processes that explicitly account for the special features of orphan medicines. Just as there are different types of approval by regulators for orphan medicines, there should be exploration of different types of decision making for orphan medicines.

But we're unconvinced about the value of many agencies essentially doing the same thing: it takes time and money to appraise orphan medicines. Doing it once, and doing well, may serve all UK patients better than the pursuit of independence for independence's sake.

Cancer52 is asking for:

Full and open approach to evaluation of changes. This should include how far proposals/changes in appraisal affect research priorities, including research for those with rare and less common cancers. Cancer52 is willing to work with all stakeholders to build on the opportunities of reform and to improve access to medicines in the UK

A debate on the merits of a single UK wide approach to appraising ultra orphan medicines

Faster decisions from agencies – patients can't always wait the time it takes for recommendations to be made

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Want to know more about what Cancer52 thinks of the policies we discuss in this paper?

Find out what Cancer52 thinks about Value Based Pricing and Value Based Assessment [here](#)

Find out what Cancer52 thinks about the Cancer Drugs Fund [here](#).