Why do 'True' Orphan Medicines Have Such a Low Acceptance Rate When Assessed by the SMC?

PSY148

P. Morten, A. Ulrich, R. Le Fevre, L.A. Eddowes

Costello Medical, Cambridge, UK

Objective

- To examine why 'true' ultra-orphan medicines have such a low acceptance rate when appraised by the Scottish Medicines Consortium as compared to the National Institute for Health and Care Excellence.

Background

- In Scotland, the Scottish Medicines Consortium (SMC) adopts a broader decision-making framework for ultra-orphan (UO) medicines, when compared to the standard SMC appraisal process.
- However, the 2016 Montgomery report found that 'true' UO (TUO) medicines have a much lower acceptance rate when appraised by the SMC as compared to other UO and end-of-life medicines.[1]

Definitions

SMC ultra-orphan medicine:
A medicine used to treat a condition with a prevalence of 1 in 50,000 or less (or around 100 people in Scotland).[2]

2016 Montgomery report 'true' ultra-orphan medicine:
A medicine appraised under the SMC ultra-orphan process and with BNF category other than 8.1 (cytotoxic drugs for Malignant Disease & Immunosuppression).[1]

BNF: British National Formulary; SMC: Scottish Medicines Consortium.

- In England, the National Institute for Health and Care Excellence (NICE) does not have a separate appraisal process for orphan medicines but may assess medicines for 'very rare conditions' via the Highly Specialised Technology (HST) process.[3]
- We compared SMC appraisals of TUO medicines, as defined by the 2016 Montgomery report, to the corresponding NICE appraisals for the same intervention-indication pairs.

Methods

- The SMC website was searched on 27 April 2017 for detailed advice for all TUO medicines using the term "ultra orphan" and excluding advice for medicines with British National Formulary category 8.1.[1, 2]
- The NICE website was subsequently searched to identify appraisals for the same intervention-indication pairs of TUO medicines appraised by the SMC.[4]
- Information concerning evidence used in these appraisals, such as incremental costs and quality-adjusted life-years (QALYs), levels of clinical evidence, patient and clinician expert opinion, and type of economic evaluation, was extracted from the respective detailed advice and final evaluation determination documents.[2, 4]

Table 1 | Comparison of SMC and NICE appraisals for 'true' ultra orphan medicines not recommended by the SMC

Drug/indication	Eculizumab		Elosulfase alfa		Ataluren	
	aHUS in adults and children		MPS IVA in patients of all ages		DMD resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 5 years and older	
	SMC 767/12	NICE HST1[a,b]	SMC 1072/15	NICE HST2[b]	SMC 1131/16	NICE HST3[b]
Outcome	Not recommended	Recommended	Not recommended	Recommended	Not recommended	Recommended
MAA or conditional on further research	N/A	Further research	N/A	MAA	N/A	MAA
PAS	✗	✗	✓	✓	✓	✓; improved in MAA
Sources of clinical evidence	Same trials used primarily		Same trials used primarily		Same trials used primarily	
'Other' sources of evidence considered	PACE	Patient and clinical expert	PACE	Patient and clinical expert	PACE	Patient and clinical expert
Non-health benefits considered	✓	✓	✓	✓	✓	✓
Type of economic evaluation	Cost-consequence	Cost-consequence	Cost-utility	Cost-consequence	Cost-utility	Cost-consequence
Annual discount rate	Not reported; varied in sensitivity analyses	1.5%	3.5%; varied in sensitivity analyses	1.5%	Not reported; varied in sensitivity analyses	3.5% (1.5% not accepted by the Committee)
Discounted incremental costs[c]	Not reported due to confidential PAS	Not reported due to confidential PAS	£8,242,197	Not reported due to confidential PAS	£4,831,312[d]	Not reported due to confidential PAS
Discounted incremental QALYs[c]	15.3	25.22	9.91	18.18	6.089	1.913 to 8.562

[a]Eculizumab was already funded via NHS England interim commissioning policy at the time of the appraisal; [b]All three HST appraisals (HST1, HST2 and HST3) were conducted prior to the recent changes to the HST process (April 2017); [c]As reported in the manufacturers' base case analyses; [d]Without PAS applied. aHUS: atypical haemolytic uraemic syndrome; DMD: Duchenne muscular dystrophy; HST: Highly Specialised Technology; MAA: managed access agreement; MPS IVA: mucopolysaccharidosis type IVA; N/A: not applicable; NICE: National Institute for Health and Care Excellence; PACE: Patient and Clinician Engagement; PAS: Patient Access Scheme; QALYs: quality-adjusted life-years; SMC: Scottish Medicines Consortium.

Results

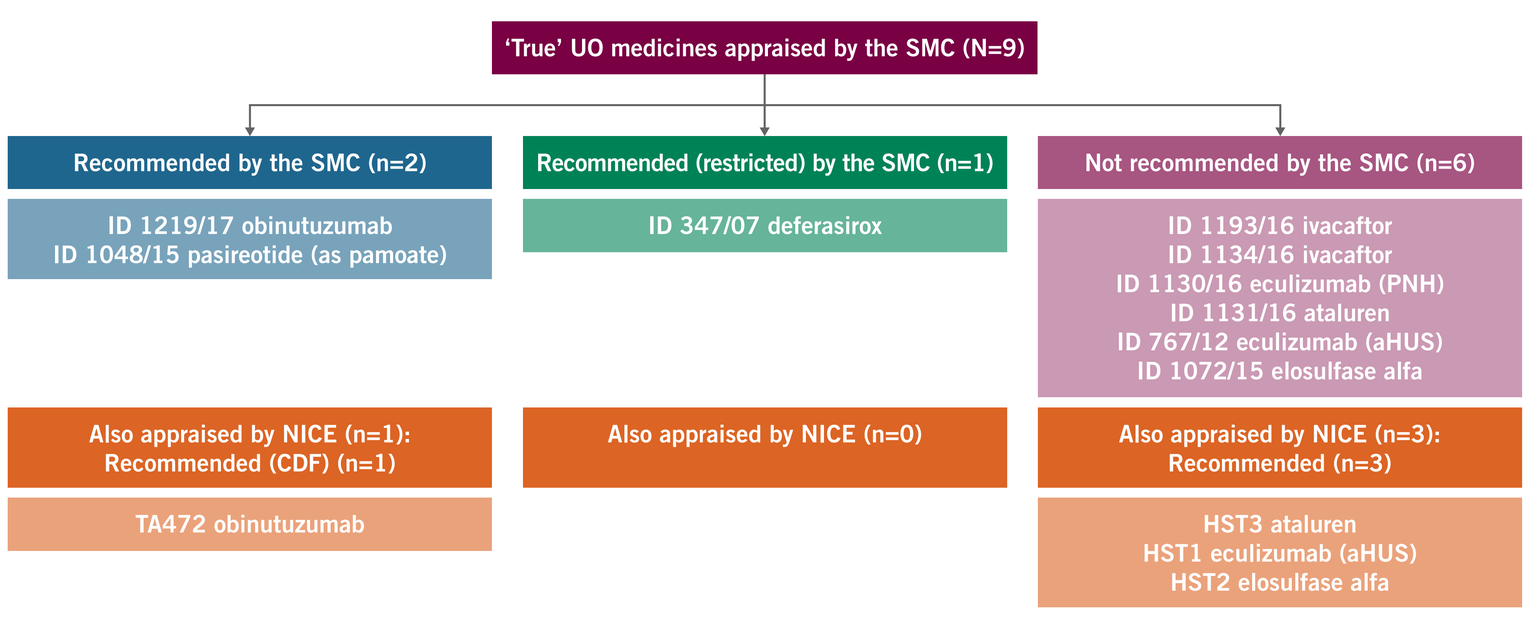
SMC appraisals of 'true' ultra-orphan medicines

- Nine TUO medicines were identified, of which only three were recommended by the SMC (33% acceptance rate) **(Figure 1)**, despite the inclusion of Patient and Clinician Engagement (PACE) meetings and SMC decision modifiers in all appraisals.
- Incremental costs were typically >£1 million in 'not recommended' appraisals and only 2/6 of these appraisals used a randomised controlled trial as a source of clinical evidence.

Comparison with NICE appraisals for 'true' ultra-orphan medicines appraised by the SMC

- Four TUO medicines appraised by the SMC were appraised by NICE **(Figure 1)**. Of those medicines not recommended by the SMC and appraised by NICE (n=3), all three were recommended by NICE via the HST process: two with a managed access agreement (MAA) and one conditional on further research **(Table 1)**.
- NICE and SMC made different recommendations despite the presentation of similar clinical evidence and consideration of both patient and clinician feedback at Evaluation Committee and PACE meetings, respectively.
- NICE HST appraisals (2/3) accepted the use of a lower annual discount rate for costs and consequences, with the QALY gain reported in these submissions tending to be higher than those in the corresponding SMC appraisal **(Table 1)**. The cost effectiveness results presented to the SMC were sensitive to the discount rate chosen (not shown here).

Figure 1 | SMC advice for 'true' ultra-orphan medicines



aHUS: atypical haemolytic uraemic syndrome; CDF: Cancer Drugs Fund; HST: Highly Specialised Technology; NICE: National Institute for Health and Care Excellence; PNH: paroxysmal nocturnal haemoglobinuria; SMC: Scottish Medicines Consortium; UO: ultra-orphan.

Conclusions

- The option to include a MAA and the acceptance of lower discount rates for costs and QALYs were key differences between NICE and SMC appraisals for TUO medicines not recommended by the SMC, and these factors most likely influenced NICE recommendations; e.g., from HST2:

  "On the basis of the available evidence on overall benefit, the Committee considered that the cost … was too high for it to be recommended outside the context of a managed access agreement."

- The option for MAAs and alternative discounting both feature in the recent changes to the NICE HST process (introduced April 2017).[3]
- The introduction of conditional recommendations, such as MAAs, as an option for SMC appraisals was recommended as part of the 2016 Montgomery report. The research here suggests that MAAs may help facilitate access to TUO medicines, specifically, as seen in England.

References

1. Montgomery B (2016). Review of Access to New Medicines. Available at: http://www.gov.scot/Publications/2016/12/9192/0 [Last accessed June 2017]; **2.** Scottish Medicines Consortium website. Available at: https://www.scottishmedicines.org.uk/ [Last accessed June 2017]; **3.** National Institute for Health and Care Excellence (2017). Interim Process and Methods of the Highly Specialised Technologies Programme. Available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf [Last accessed August 2017]; **4.** National Institute for Health and Care Excellence website. Available at: https://www.nice.org.uk/ [Last accessed June 2017].

Appraisal documents for each of the nine SMC appraisals and corresponding NICE appraisals were downloaded from the respective websites.

Acknowledgements

The authors thank Mark Tassell, Costello Medical, for graphic design assistance.

Presented at the ISPOR 20th Annual European Congress | Glasgow, UK | 4–8 November 2017