Reappraisal following the loss of medicine patent in health technology assessment guidelines

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INTRODUCTION

Loss of patent for a medicine often means a lower price, due to increased manufacturing competition. Whilst the impact of the loss of patent on price levels is relatively well researched, there is less evidence on the impact for HTA decision making when a medicine becomes unbranded.

We aimed to explore whether HTA guidance should be updated when: (i) A medicine that had originally received a negative recommendation becomes unbranded and has a lower price, (ii) An original medicine was not appraised but is now off patent, and (iii) A comparator treatment in an original appraisal is now unbranded and has a lower price.

METHODS

The first stage of the project was to identify a sample of completed NICE Single Technology Appraisals (STAs) that had resulted in the intervention being not recommended by the NICE Appraisal Committee (AC) (that is, not even an optimised recommendation). The appraisal documents were examined to understand the feasibility of using the historic clinical and economic evidence, including the economic models, to 'pragmatically assess' whether an unbranded version of the originator technology appearing on the market today (at a lower price) would be recommended (or, in the case of an optimised recommendation, be recommended to a wider population). MTAs were not included in the assessment.

We examined the Final Appraisal Determination (FAD) documents, issued during a ten-year period, for all STAs that resulted in a 'not recommended' or optimised recommendation. The aim was to identify a mixture of decision types and disease areas to assess the following questions:

- To what extent have the treatment pathway, resource use (and costs), comparators, (including availability and costs of unbranded versions of comparators) changed since the introduction of the guidance?
- What new evidence has been published about the originator drug? The goal was not to review the evidence but to identify it so that we could understand the extent to which the evidence that had been assessed during the original appraisal would need to be updated.
- Whether the models that had been developed to inform the original appraisal were available and whether they could be used to assess the cost-effectiveness of a biosimilar (and whether any confidential evidence used to populate the models is now in the public domain).

In addition, in a separate exercise, documentation associated with all STAs that had resulted in a technology not being recommended or given an optimised recommendation between 2010 and 2016, were examined to determine whether the technology had later been recommended. Research was also undertaken to determine whether a new technology had been recommended for the same population, thus leading to either a change of relevant comparator(s) or treatment pathway.

Table 1: Summary of findings

ID	Justification for recommendation	Key cost drivers		QALY drivers		Additional data published from pivotal trial	Changes in pathway since STA	Is rapid assessment of a biosimilar feasible using existing submission?
		Changed since publication	Ability to change in model	Key driver	Ability to change in model			
1	Not cost-effective. Uncertain clinical evidence.	Minor	Yes	PFS and OS	Yes. Partitioned survival model that will accept new OS and PFS curves	Yes. Final OS and PFS data published showing no difference in OS.	No	A rapid assessment would be feasible using the existing model, after it had been updated with new clinical evidence from the pivotal trial
2	Not cost-effective	Minor	Yes	OS	Yes. Markov model so transition probabilities easy to change.	There were no pivotal trials	Yes. New comparator.	No. Comparison of a biosimilar with the new comparator would be required.
3	Not cost-effective. Uncertain clinical evidence.	Minor	Yes	Maintenance of remission	Yes. Markov model so transition probabilities easy to change.	No	Yes. Change in maintenance therapy when achieving remission	No. The weak evidence base and change in subsequent therapies means that a rapid assessment would not be possible
4	Not cost-effective. Uncertain clinical evidence.	No but one of the comparators comes off patent in 2021 meaning it may fall in price soon.	Yes (although unclear if this would be case in the ERG model)	OS	Yes. Partitioned survival model that will accept new OS and PFS curves	No	A later appraisal did recommend the intervention and a new therapy further in the pathway (third line) has been recommended	No. The weak evidence base means that a rapid assessment would not be possible and subsequent treatments have changed. Also, the ERG model not made available.
5	Not cost-effective. Uncertain clinical evidence.	No	Yes (although unclear if this would be case in the ERG model)	OS	Yes. Would need a change in response rates which is easy to implement.	No	No	No. The weak evidence base and model limitations mean that a rapid assessment would not be possible. The ERG model was not made available.
6	Not cost-effective. Model structure unsuitable for decision making. Uncertain clinical evidence. Implausible assumptions in the model.	No	Yes	Utility loss from future treatments	Yes. Would need a change in response rates which is easy to implement.	No	No	No. The weak evidence base and model limitations mean that a rapid assessment would not be possible.
7	Not cost-effective. Uncertain clinical evidence.	No	Yes	OS	Yes. Partitioned survival model that will accept new OS curves	No (still ongoing)	No	No. The weak evidence base and model limitations mean that a rapid assessment would not be possible.

RESULTS AND CONCLUSIONS

We were able to examine documents associated with nine STAs. Two of the included STAs, whilst identified as resulting in optimised recommendations, were recommendations for the full population in the appraisal scope. Whilst, in theory, the same process could have been undertaken for these appraisals as for the STAs where the technology was not recommended (or genuinely optimised), we considered that where full recommendations had been given then, by default, the NICE AC must have been satisfied that the evidence and the results generated by the economic model were reliable and, therefore, could be used to inform decision making. As such, little could be learned from a review of these STAs.

A summary of our findings from the seven reviewed STAs is presented in Table 1. Of the seven reviewed STAs, only one was considered to be of suitable potential to be used as the basis for a rapid assessment of an unbranded version of the originator. In the other six cases, we considered that a rapid assessment would not possible because it was likely that a NICE AC would need to reconsider the historic evidence with the new price for one or more of the following reasons:

- The pathway had changed, meaning that new clinical evidence would be required.
- The NICE Appraisal Committee had not been convinced by the clinical effectiveness evidence for the originator.
- The model was unreliable due to: structural flaws; implausible assumptions; or included errors that could not be rectified by the ERG.

Whilst there is potential to use models from previous STAs for method development, they cannot be used for other reasons without first getting permission from the submitting company.

Of 85 STAs (with FADs published between 2010 and 2016), that resulted in a negative or optimised recommendation, 68 (82.9%) were either recommended as a consequence of a later submission (n=8) or an STA resulted in a recommendation for a different technology leading to a change of relevant comparator and/or pathway (n=60).

Of the fifteen STAs that resulted in a negative or optimised recommendation and where no further recommendations were made, four were of technologies that had no patent. Of the remaining eleven, six were of technologies that had patents that had recently expired or were due to expire within the next three years.

Based these findings, it seems unlikely that there will be many opportunities to undertake rapid assessment of unbranded versions of originator technologies with negative or optimised recommendations during the next few years through use of the originator STA evidence.

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