ABPI Member Survey

August 2021

Reasons for NICE 'Optimised' Recommendations and Terminated Appraisals

Introduction

Over the last 20 years, 82% of technology appraisal recommendations have been 'positive' (recommended or optimised) (NICE, 2020); around one third of these are 'optimised' recommendations, though this has risen in the past five years to account for around 43% of positive recommendations.

Given the significant proportion of positive NICE recommendations that are optimised, last year the ABPI funded a project by the Office of Health Economics (OHE) which quantified the level of patient access associated with NICE optimised recommendations between 2015 and 2019. This involved (where sufficient information was available within the appraisal documentation) a comparison between the patient group recommended treatment, and the full licensed population for the indication under review (Bulut, O'Neill and Cole, 2020). The study found that for about two-thirds of optimised recommendations evaluated, NICE recommended use for less than half of eligible patients relative to license; around one-third (35%) recommended use in less than a quarter of patients within NICE's appraisal scope. On average, 39% of the patient population that was potentially eligible for the treatment under review were recommended for treatment in NICE's optimised recommendation (Bulut, O'Neill and Cole, 2020).

In order to better understand the reasons for optimised recommendations, the ABPI issued a survey to member companies in March 2021, requesting details of appraisals with an optimised recommendation (including optimised CDF recommendations) over the last five years (2016 – 2021). In addition, the survey requested information on terminated appraisals within the same time period, to gather information on the main reasons for non-submission of evidence by companies.

NICE optimised recommendations

Details of 48 technology appraisals (TAs) were received, which represents around 45% of all optimised recommendations over the last five years (NICE, 2020)[1]. Characteristics of the sample are provided in Table A1(A) in the Appendix.

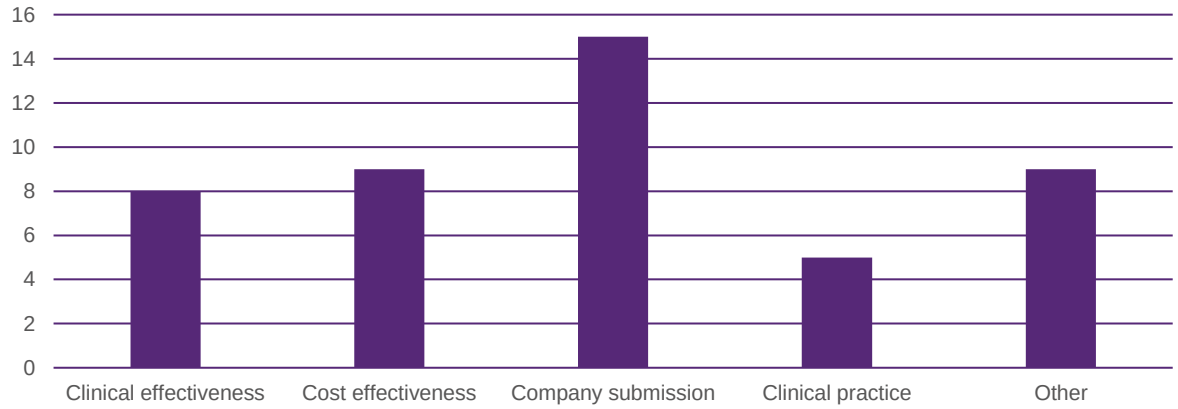
Survey respondents were asked to select – from a drop-down menu – the main reason for the optimised recommendation. Results are presented in Table 1 and Figure 1 below.

Table 1: Main reason for the NICE optimised recommendation

REASON	NUMBER	% SAMPLE*
Clinical effectiveness: Lack of evidence of clinical effectiveness in full licensed population (determined by NICE)	8	17%
Cost effectiveness: Determined by NICE to be clinically superior in full licensed population, but not found to be cost effective in full licensed population.	9	20%
Company submission: Company did not submit clinical/cost effectiveness evidence for full licensed population	15	33%
Clinical practice: Stratification of the patient population (e.g., according to line of therapy) to reflect clinical practice	5	11%
Other	9	20%
TOTAL	46	

*% of sample for which information was provided: 46 (two entries did not provide the reason). NOTE: Information provided by survey respondents was not independently verified; therefore, results summarise the submitting company's impression of NICE's main motivation for optimising the recommendation.

Figure 1: Main reason for the NICE optimised recommendation



[1] According to NICE there were 108 TAs with optimised recommendations between 2016 and March 2021.

According to the submitting companies, over the last five years the main reason for NICE's restrictive recommendation relative to license is that the company did not submit clinical/cost effectiveness evidence for the full licensed population. The next most prevalent reason was cost-effectiveness (20%), clinical-effectiveness (17%) and stratification of the patient population to reflect clinical practice (11%). 'Other' reasons mainly comprised a combination of the other options. Whilst 'company submission' was the most highly cited reason for the optimised recommendation, ABPI's members commented in practice this represents the companies' *expectation* of a positive NICE recommendation in only a subset of patients (relative to license), given one of (or a combination of) the other reasons, usually that the medicine will not be considered cost-effective in the licensed population.

Tables A1(B-D) in the Appendix present subgroup-analyses of the reasons for the optimised recommendation. Some notable differences include:

- Optimisation due to clinical effectiveness appears to be more prevalent for solid cancers compared with haematological cancers, whereas reasons of 'clinical practice' (stratification of the patient population e.g., according to line of therapy to reflect clinical practice) are much more common for haematological cancers.
- Optimisation due to the company's submission of evidence is a more prevalent reason for subsequent indications compared with new active substances.
- Restrictions on access to end-of-life drugs are more commonly for reasons of clinical and cost-effectiveness, whereas company submission is the most important reason for non-end-of-life drugs.

NICE Terminated Appraisals

The technology appraisal process is based on the manufacturer's submission of evidence. In the absence of a submission by the manufacturer, the NICE appraisal is terminated, and a recommendation is not made. There is no or very little information made public on the reason for non-submissions. To shed some light on this, the survey issued to member companies included questions around the reason for non-submission of evidence for terminated appraisals over the last five years (2016 – 2021). The characteristics of the 30 terminated appraisals (approximately 79% of all terminated appraisals over the time period[2]) that were captured in the sample of survey responses are provided in Table A2 in the Appendix.

Survey respondents were asked to select – from a drop-down menu[3] – the main reason for the terminated appraisal. Results are presented in Table 2 and Figure 2 below.

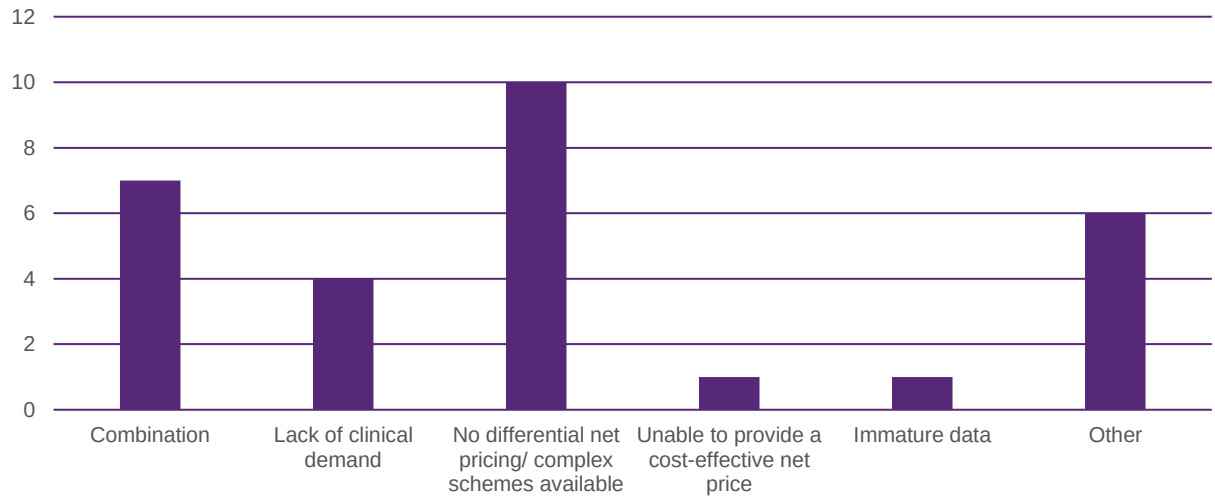
[2] According to NICE there were 38 terminated appraisals between 2016 and March 2021, however these include those reported as suspended and no intention to submit.
[3] There were four 'reasons' offered that were not selected by any respondent: "*Inflexibility of NICE engagement processes resulted in too much uncertainty regarding how to prepare a submission"; "Return does not justify resource/cost of preparing submission";*

Table 2: Main reason for the terminated appraisal (non-submission)

REASON	NUMBER	% SAMPLE*
Combination: unable to present a cost-effective case due to pricing of other medicines in the combination.	7	24%
Lack of clinical demand: no positioning of product on English clinical pathways	4	14%
No differential net pricing/complex schemes available: Lack of flexibility to pursue differential net pricing or complex schemes, with consequent risk to previously approved indications	10	34%
Unable to provide a cost-effective net price	1	3%
Immature data: Too much clinical uncertainty due to immature data	1	3%
Other	6	21%
TOTAL	29	

*% of sample for which information was provided: 29 (one entry did not provide the reason). NOTE: Results summarise the submitting company's recall of the main motivation for non-submission of evidence, leading to a terminated appraisal.

Figure 2: Main reason for the terminated appraisal (non-submission)



"Concern regarding transparency of pricing information that will go into the public domain upon publication of the appraisal"; and "No CDF option to support early submission where there is significant uncertainty". The fact that no respondent selected any of these options reflects well on the NICE process itself.

According to survey respondents, over the last five years the main reason for non-submission of evidence, leading to a terminated appraisal, was the lack of flexibility to pursue differential net pricing or complex schemes, with consequent risk to the revenue from previously approved indications (34%). The second most prevalent reason was *'combination - unable to present a cost-effective case due to pricing of other medicines in the combination*' (24%). Taking these together, it is clear that a major reason (representing around 60% of all responses) for non-submission of therapies for NICE appraisal is the inability for companies to offer a differential net price that could enable cost-effectiveness of the treatment, and therefore uptake, whether as mono-therapy or in combination with another branded product. This rises to 68% if we consider only those therapies representing "subsequent indications", which represent 86% of the sample (compared with 53% in the NICE optimised recommendations survey sample). Lack of clinical demand represented 14% of responses; those selecting 'other' mainly described a combination of the other factors.

Conclusion

While the survey results may not be fully representative as they do not include all optimised or terminated technology appraisals over the last five years, they offer a helpful insight into companies' observations and motivations, particularly for terminated appraisals for which there is very little information publicly available.

It is also interesting to compare characteristics of the sample. For example, medicines indicated for solid tumours represented the largest group among optimised recommendations (46%), whereas – among terminated appraisals – medicines for haematological cancers represented by far the largest group (53%). Among terminated appraisals there were more therapies targeting rarer conditions, and a greater proportion of follow-on indications.

Appendix

Table A1(A): Characteristics of survey sample of NICE Technology Appraisals with an optimised recommendation

	NUMBER	% SAMPLE*
THERAPY AREA		
Solid cancer	22	46%
Haematological cancer	10	21%
Immunology	6	13%
Metabolic	1	2%
Other non-cancer	9	19%
PREVALENCE		
Common	19	49%
Small indication but not orphan	10	26%
Orphan	8	21%
Ultra-orphan	2	5%
NEW OR FOLLOW-ON INDICATION		
New active substance	22	47%
Subsequent indication	25	53%
COMBINATION		
Combination therapy (branded/branded)	8	18%
Not combination (branded/branded)	36	82%
END OF LIFE		
End of life appraisal	17	37%
Not end of life appraisal	29	63%
TOTAL SAMPLE	**48**	

*% of sample for which information was available for the relevant characteristic. NOTE: Not all categories total to the full 48 in our sample, due to some missing information.

Table A1(B): Main reason for the NICE optimised recommendation: sub-group analysis by therapy area

	Solid cancer %(N)	Haem cancer %(N)	Immunology %(N)	Metabolic %(N)	Other non-cancer %(N)	Total (N)
Clinical effectiveness: Lack of evidence of clinical effectiveness in full licensed population (determined by NICE)	25% (5)	10% (1)	17% (1)	0	11% (1)	8
Cost effectiveness: Determined by NICE to be clinically superior in full licensed population, but not found to be cost effective in full licensed population.	20% (4)	30% (3)	17% (1)	0	11% (1)	9
Company submission: Company did not submit clinical/cost effectiveness evidence for full licensed population	25% (5)	30% (3)	33% (2)	0	56% (5)	15
Clinical practice: Stratification of the patient population (e.g., according to line of therapy) to reflect clinical practice	5% (1)	30% (3)	0	100% (1)	0	5
Other	25% (5)	0	33% (2)	0	22% (2)	9
TOTAL (N)	20	10	6	1	9	46

Table A1(C): Main reason for the NICE optimised recommendation: sub-group analysis by NAS/subsequent indication

	New active substance %(N)	Subsequent indication %(N)	TOTAL (n)
Clinical effectiveness: Lack of evidence of clinical effectiveness in full licensed population (determined by NICE)	18% (4)	17% (4)	8
Cost effectiveness: Determined by NICE to be clinically superior in full licensed population, but not found to be cost effective in full licensed population.	27% (6)	13% (3)	9
Company submission: Company did not submit clinical/cost effectiveness evidence for full licensed population	27% (6)	38% (9)	15
Clinical practice: Stratification of the patient population (e.g., according to line of therapy) to reflect clinical practice	14% (3)	8% (2)	5
Other	14% (3)	25% (6)	9
TOTAL (N)	22	24	46

Table A1(D): Main reason for the NICE optimised recommendation: sub-group analysis by end of life/not end of life therapy

	End of life %(N)	Not end of life %(N)	TOTAL (n)
Clinical effectiveness: Lack of evidence of clinical effectiveness in full licensed population (determined by NICE)	24% (4)	14% (4)	8
Cost effectiveness: Determined by NICE to be clinically superior in full licensed population, but not found to be cost effective in full licensed population.	29% (5)	14% (4)	9
Company submission: Company did not submit clinical/cost effectiveness evidence for full licensed population	18% (3)	41% (12)	15
Clinical practice: Stratification of the patient population (e.g. according to line of therapy) to reflect clinical practice	12% (2)	10% (3)	5
Other	18% (3)	21 (6)	9
TOTAL (N)	17	29	46

Table A2: Characteristics of survey sample of NICE terminated technology appraisals

	NUMBER	% SAMPLE*
THERAPY AREA		
Solid cancer	8	27%
Haematological cancer	16	53%
Immunology	4	13%
Other non-cancer	2	7%
PREVALENCE		
Common	5	18%
Small indication but not orphan	8	29%
Orphan	12	43%
Ultra-orphan	3	11%
NEW OR FOLLOW-ON INDICATION		
New active substance	4	14%
Subsequent indication	25	86%
COMBINATION		
Combination therapy (branded/branded)	9	30%
Not combination (branded/branded)	21	70%
TOTAL SAMPLE	**48**	

*% of sample for which information was available for the relevant characteristic. NOTE: Not all categories total to the full 48 in our sample, due to some missing information.

References

Bulut, M., O'Neill, P. and Cole, A., 2020. *NICE 'Optimised' Decisions: What is the Recommended Level of Patient Access?* [OHE Consulting Report,] London: Office of Health Economics. Available at: https://www.ohe.org/publications/nice-%E2%80%98optimised%E2%80%99-decisions-what-recommended-level-patient-access#

NICE, 2020. *Technology appraisal data: appraisal recommendations*. [online] NICE. Available at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/data/appraisal-recommendations [Accessed 16 Mar. 2021].