

## INTRODUCTION

It is well known that health providers around the world are being confronted with rising demand for expensive new therapies, whilst also facing restrictions on their purchasing budgets and pressure to maximize efficiency and minimize costs.

In the UK, the National Institute for Health and Clinical Excellence (NICE) is at the forefront of evaluating the clinical and cost-effectiveness of new therapies and advising on their adoption by the National Health Service (NHS) accordingly.

Manufacturers have begun to utilize Innovative Pricing Agreements (IPAs), referred to by NICE as Patient Access Schemes, within their submissions to improve patient access to new medicines.

## OBJECTIVES

- Identify all IPAs from published NICE appraisals between 2000 and 2009.
- Analyze the submissions to discern similarities and differences between the IPAs of various appraisals.
- Provide recommendations to pharmaceutical companies on using IPAs in NICE submissions.

## METHODS

Two individuals reviewed all completed NICE technology appraisals published between 2000 and 2009. <http://guidance.nice.org.uk>

Each technology appraisal was searched for the presence of an IPA by reading the Guidance section of the appraisal and searching the document for the phrases 'patient access' and 'innovative pricing.' Submissions that were withdrawn or had their appraisal terminated were excluded from the analysis.

An IPA was defined as the manufacturer providing a pre-defined reduction of the overall cost of treatment based on risk-sharing.

The technology appraisals were analyzed by two individuals to identify the disease indication, type of IPA and cost per quality adjusted life year (QALY) gained for the therapy with and without the inclusion of the IPA (where reported).

## RESULTS

**Table 1. Summary of all published technology appraisals containing IPAs up to the end of 2009**

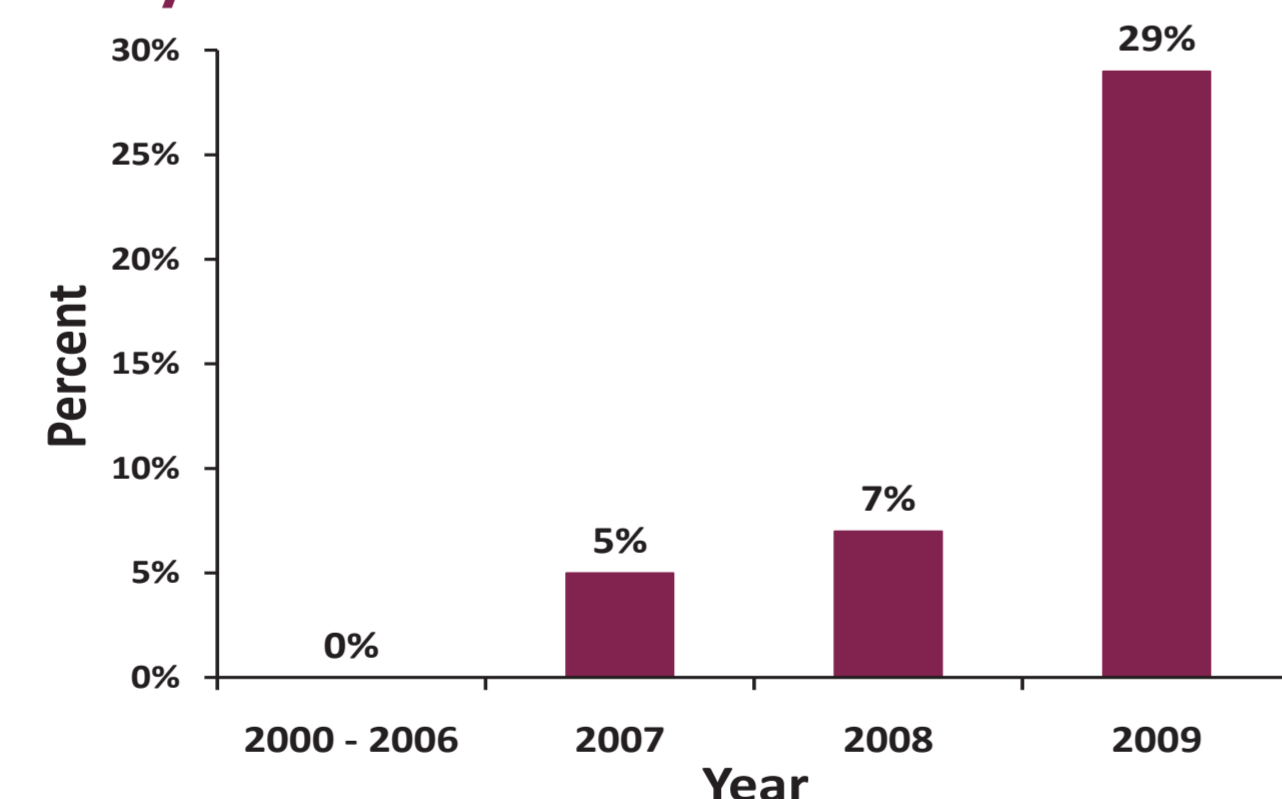
Year	NICE Technology Appraisals		Drug (TA number)	Therapeutic Area	IPA Category*	Details of the Innovative Pricing Agreement
	Total N <sup>o</sup>	N <sup>o</sup> With IPA				
2007	21	1	<b>Bortezomib</b> (TA129)	Multiple myeloma	1	Manufacturer rebates the full cost for those with a less than partial response after 4 cycles of treatment
2008	27	2	<b>Erlotinib</b> (TA162)	Non-small cell lung cancer	2	Manufacturer provides an overall treatment cost equal to that of docetaxel
			<b>Ranibizumab</b> (TA155)	Wet age-related macular degeneration	3	Cost of ranibizumab beyond 14 injections in the treated eye is met by the manufacturer
2009	17	5	<b>Sunitinib</b> (TA179)	Gastrointestinal stromal tumour	4	Drug cost of sunitinib for the first treatment cycle will be met by the manufacturer
			<b>Ustekinumab</b> (TA180)	Psoriasis	1	Manufacturer provides 90 mg dose (for people weighing > 100 kg) at same total cost as the 45 mg dose
			<b>Cetuximab</b> (TA176)	Colorectal cancer	1	Manufacturer rebates 16% of the amount of cetuximab used on a per patient basis.
			<b>Lenalidomide</b> (TA171)	Multiple myeloma	3	Drug cost for those receiving treatment for more than 26 cycles will be met by the manufacturer
			<b>Sunitinib<sup>1</sup></b> (TA169)	Advanced /metastatic renal cell carcinoma (first line)	4	Drug cost of sunitinib for the first treatment cycle will be met by the manufacturer

**IPA Category Key:** 1 Rebate across a patient population (n=3), 2 Cost matched to existing treatment (n=1), 3 Dose-capping (n=2), 4 Free provision of first treatment cycle (n=2)

<sup>1</sup> Following this publication (March 2009), sunitinib was also appraised as part of a multiple-technology appraisal (MTA) for advanced/metastatic renal cell carcinoma, for second-line indication (August 2009). This published submission also included an IPA, but received a negative appraisal from NICE. This MTA has been excluded from this analysis to avoid repeated inclusion of sunitinib for the indication of renal cell carcinoma.

The percentage of published NICE technology appraisals containing IPAs increased over time, from 0% in 2000-2006 to 29% in 2009 (Table 1 and Figure 1).

**Figure 1. Percentage of Published Appraisals with IPAs by Year**



Of the 8 IPAs identified, 6 (75%) were for oncology products, 1 (12.5%) was for psoriasis and 1 (12.5%) was for wet age-related macular degeneration.

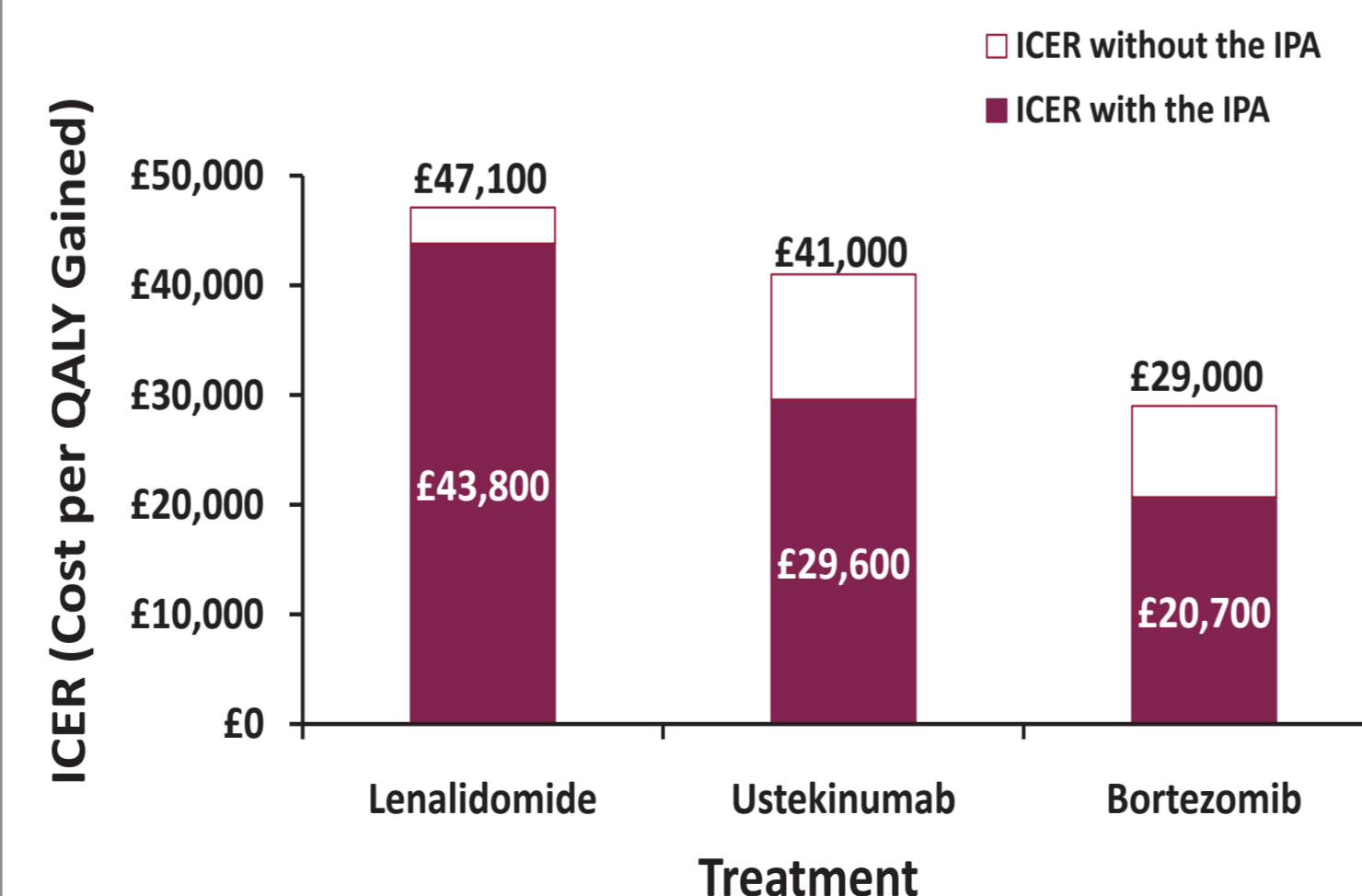
In 4 cases, IPAs were part of the initial submission, in 3 other cases they were part of a revised manufacturer's model and in 1 case the IPA was proposed by the NICE committee.

Seven of the IPAs were based on pre-defined budget caps or discounts (Table 1). The IPA for bortezomib was an outcome-based scheme, with rebates provided for non-responding patients.

Figure 2 compares the Incremental Cost-Effectiveness Ratio (ICER) (cost per QALY gained) for 3 treatments, with and without their IPAs.

The inclusion of an IPA reduced the ICER of ustekinumab by 28% and bortezomib by 29%. The inclusion of an IPA in the case of lenalidomide had a smaller effect on the ICER, with a reduction of only 7%. This did not bring the ICER below the standard supposed £30,000 NICE Willingness-To-Pay (WTP) threshold. However, lenalidomide was considered to meet NICE's end-of-life criteria, where the standard WTP threshold may be exceeded.

**Figure 2. Change in cost-effectiveness after inclusion of an IPA**



## DISCUSSION

The Multiple Sclerosis Risk Sharing Scheme (initiated in 2002) was the first example of a risk-sharing scheme in the UK. The 10-year scheme, conducted on a local level, involves direct agreement between the manufacturer and the Primary Care Trusts. From 2007 to 2009 such schemes have been adopted at the national level, as demonstrated by the inclusion of IPAs in 8 NICE technology appraisals in this period.

It has been categorically stated by the Department of Health that IPAs should be the "exception rather than the rule" in drug appraisals (*Pharmaceutical Price Regulation Scheme 2009*. [http://www.dh.gov.uk/en/PublicationsandStatistics/Publications/PublicationsPolicyAndGuidance/DH\\_091825](http://www.dh.gov.uk/en/PublicationsandStatistics/Publications/PublicationsPolicyAndGuidance/DH_091825)). The inclusion of IPAs in submissions to NICE does not necessarily guarantee positive guidance.

The increase in IPAs in NICE appraisals is likely to be a reaction to the pressure faced by health authorities to provide access to new treatments, whilst simultaneously reducing their spending and minimizing the uncertainty of treatment costs. The IPAs have most commonly been employed in appraisals of innovative cancer therapies, an area well recognised for high costs and patient access limitations in the UK.

### Discussion continued.

Our study has several limitations. We could only identify completed NICE technology appraisals and as such we were unable to analyze the percentage of withdrawn appraisals that also contained IPAs. Furthermore, details of the cost-effectiveness for treatments with and without IPAs were only available for lenalidomide, ustekinumab and bortezomib, thereby restricting the analysis of cost per QALY gained to these three appraisals. However, from these results alone we can recognize the value of IPAs in improving the cost-effectiveness figure of a treatment in a specific market, and addressing some of the uncertainties to the payer.

IPAs provide an opportunity to enhance market access for products that may otherwise be restricted due to various factors, including cost and uncertainty related to clinical outcomes. Manufacturers should ensure that any NICE submissions including IPAs are corroborated by well-designed clinical trials to provide strong clinical efficacy data, as well as developing a robust economic model to support the application. The IPAs should also be in line with the value story of the new medication. For example, the IPA for ranibizumab reflects the fact that the clinical benefit will be seen within 14 injections.

From our analysis, it would seem that outcome-based IPAs (such as the IPA for bortezomib) are rare. This may be because non outcome-based schemes can be associated with a lower administrative burden, as they require minimal patient or physician reporting. This warrants further research, but manufacturers should bear this in mind when proposing IPAs. Manufacturers should also note that if they wish to propose an IPA in a submission to NICE, then it should be included at the outset (*PPRS 2009*).

We propose to review this research at the end of 2010 as it seems likely that the trend identified will continue. It is of note that both of the positive technology appraisals released by NICE so far this year (up to March 2010), include an IPA:

- Trabectedin for the treatment of advanced soft tissue sarcoma (IPA category 3)
- Certolizumab pegol for the treatment of rheumatoid arthritis (IPA category 4)

From the documentation available there are 11 NICE appraisals expected to be released in the remainder of 2010, of these, 5 currently include IPAs (all 5 of which are for oncology products).

NICE is seen as a leader in terms of health technology appraisals and health economics on the international stage; thus this trend for increased use of IPAs may have implications at a global level. Further research to explore the patterns of IPA-inclusion in submissions to health authorities outside the UK could therefore be worthwhile.

## CONCLUSIONS

Pharmaceutical companies are increasingly using innovative pricing agreements in their NICE submissions, and this trend looks set to continue. Such agreements are mutually beneficial and acceptable to both parties and can enhance the market access of innovative therapies.