# EXPLORING THE VARIABILITY BETWEEN DISEASE TYPE AND THE PROPORTION OF SUBMISSIONS WITH ICERS LOWER THAN THE THRESHOLD THAT ARE REJECTED BY HTA AGENCIES

PAREXEL®
YOUR JOURNEY. OUR MISSION.™

SCM Walsh
& EA Griffiths

HERON™
Commercialization

## INTRODUCTION

Health technology assessments (HTAs) are used in many countries to assess the value of newly licensed medicines and devices. HTA agencies use varying criteria, generally surrounding clinical and cost-effectiveness, to decide whether or not to recommend new treatments for reimbursement.[1]

Cost-effectiveness is often based on incremental cost-effectiveness ratios (ICERs)[1], and agencies typically use a threshold (around £30 000 for NICE and SMC; AUS$42 000 for PBAC; and CAD$50 000 for CADTH) as the limit for acceptance. However, treatments may be rejected despite having ICERs lower than the usual threshold[2], and the decision drivers in such circumstances may vary by disease area.

## AIM

**To inform future submissions, we assessed the proportion of rejected submissions with ICERs lower than the threshold by disease area, and examined any variability in the decision drivers surrounding rejection.**

## METHODS

All HTA appraisals from January 2000 to January 2014 from HTA agencies in 4 countries were included in the analysis:

- Australia: Pharmaceutical Benefits Advisory Committee (PBAC)
- Canada: Canadian Agency for Drugs and Technologies in Health (CADTH)
- England: National Institute for Health and Care Excellence (NICE)
- Scotland: Scottish Medicines Consortium (SMC)

Multiple technology appraisals, vaccination programs, requests for advice, and submissions for which an ICER could not be determined were excluded from the analysis. Appraisals were categorized by British National Formulary (BNF) disease type and the full responses were reviewed; the submitted ICER, recommendation, and reasoning behind the recommendation were extracted.

Appraisals that were accepted either in line with the submission or in a restricted population were classified as accepted. Appraisals that were not recommended were classified as rejected. More than one reason could be selected as a key decision driver for each reimbursement decision. Where multiple base case ICERs were submitted, the manufacturer's most relevant ICER was extracted, according to the proposed indication of the drug.

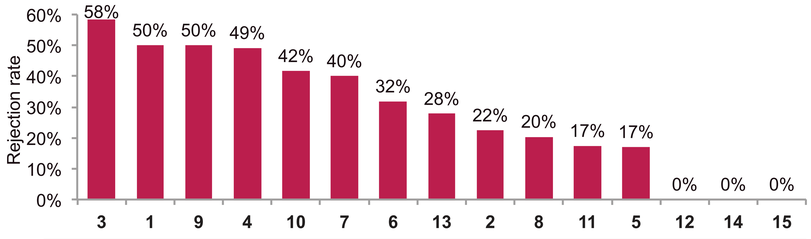
## RESULTS

### *Rejection by BNF category*

Across all four agencies, 679 submissions met the inclusion criteria. 428 submissions had a lower than threshold ICER, and 128 (30%) of these submissions were rejected. Submissions with ICERs lower than the threshold were less likely to be rejected than those with ICERs above the threshold (p<0.0001).

The proportion of rejected submissions with ICERs below the threshold varied by disease type. The top three disease categories for rejection despite an ICER below the threshold were: respiratory system (58%); gastrointestinal system (50%); and nutrition and blood (50%). The three disease areas with the lowest proportion of rejected submissions despite an ICER below the threshold were: infections (17%); eye (17%); and malignant disease and immunosuppression (20%) (FIGURE 1).

**Figure 1. Rejection rates of submissions with lower than threshold ICERs, by BNF category***




| | 3 | 1 | 9 | 4 | 10 | 7 | 6 | 13 | 2 | 8 | 11 | 5 | 12 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| n | 7 | 8 | 6 | 29 | 10 | 2 | 14 | 5 | 13 | 22 | 4 | 8 | 0 | 0 | 0 |
| N | 12 | 16 | 12 | 59 | 24 | 5 | 44 | 18 | 58 | 108 | 23 | 47 | 0 | 0 | 0 |

***BNF categories:**

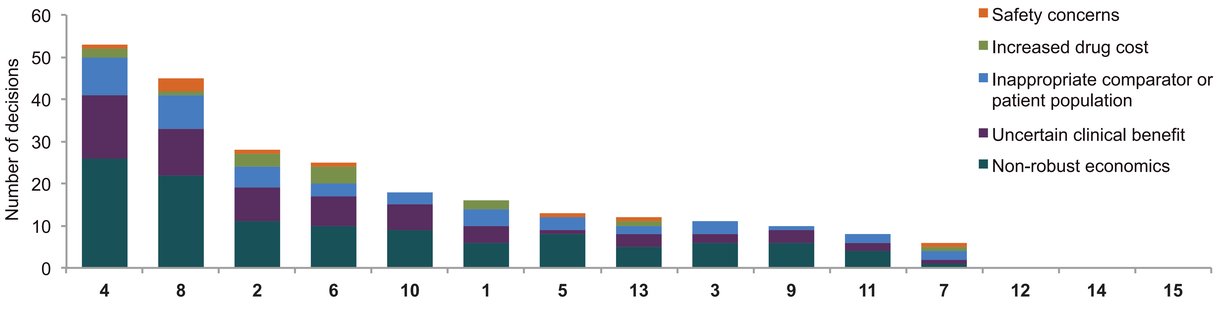
1 Gastrointestinal System
2 Cardiovascular System
3 Respiratory System
4 Central Nervous System
5 Infections
6 Endocrine System
7 Obstetrics, gynecology, and urinary-tract disorders
8 Malignant disease and immunosuppression
9 Nutrition and blood
10 Musculoskeletal and joint diseases
11 Eye
12 Ear, nose, and oropharynx
13 Skin
14 Immunological products and vaccines
15 Anesthesia

### *Rationale for rejection*

Overall, the most frequent reason for rejection despite a lower than threshold ICER was non-robust economic analysis (accounting for 47% of all recorded decisions). Other key decision drivers for rejection included: uncertain clinical benefit (26% of decisions); use of an inappropriate comparator or patient population (18%); increased drug cost (6%); and safety concerns (4%).

Trends in reasons for rejection were generally consistent across disease areas, with non-robust economic analyses accounting for the highest proportion of decision drivers across nearly all disease categories (FIGURE 2).

**Figure 2. Decision drivers behind rejection of submissions with lower than threshold ICERs, by BNF category***




## DISCUSSION

Across the four HTA agencies, 30% of submissions with submitted ICERs lower than the threshold were rejected. The proportion of rejected submissions varied widely by disease type, though non-robust economic analysis was the most prevalent reason for rejection across all but one disease categories. This may indicate a need for more convincing health economic modelling in some therapy areas.

Understanding the rationale behind the recommendations given by HTA agencies should allow manufacturers to maximize the likelihood of a positive outcome, by considering historic trends across disease categories and presenting submissions accordingly.

The evidence suggests that a low ICER is not sufficient to offset a weak economic analysis, regardless of disease area, reinforcing the view that HTA submissions should be supported by a robust clinical and economic argument in order to avoid a negative reimbursement decision.

## CONCLUSION

**The proportion of submissions with lower-than-threshold ICERs that were rejected varied widely by disease type. The key driver of rejection across disease categories was non-robust economic analysis. HTA submissions should be supported by transparent and robust economic and clinical evidence, regardless of disease area.**

## REFERENCES

1. NICE (2014) Guide to the methods of technology appraisal
2. Walsh SCM & Goodrich K (2013) Exploring the key decision drivers provided by HTA agencies rejecting submissions with ICERs lower than the threshold. ISPOR 16th Annual European Congress

PAREXEL International
195 West Street
Waltham, MA 02451 USA
+ 1 781 487 9900
www.PAREXEL.com