Are Accelerated Approval Mechanisms a Predictor to Early Access and Coverage? A Global Study of Cancer Drugs

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Background
- Accelerated regulatory pathways created by the FDA in the US, the EMA in the EU and other regulators have the capacity to dramatically change the patient treatment paradigm. Drugs that are of major interest for public health or that are therapeutic innovations may be subject to these accelerated approval procedures; cancer treatments are key among these.
- Aim: To explore the interrelationship between accelerated approval schemes for cancer drugs and national HTA processes across four jurisdictions globally (England, Scotland, Australia and Canada), by investigating the impact HTA and value assessment has on drugs approved through accelerated pathways.

Methods
- 16 drug-indication pairs with cancer indications (melanoma, lung and haematology) were selected based on whether they received accelerated approval in the US or Europe via one of the FDA Accelerated Approval pathways or the EMA Conditional Marketing Authorisation (CMA), or both, until December 2015.
- In-depth analysis of HTA impact on coverage and funding pathways in the four selected countries relied on an analytical methodology framework investigating: (a) Similarities and differences in clinical and economic evidence submitted; (b) Evidence interpretation; (c) Uncertainties; (d) Other considerations, drug or therapeutic-area related; and (e) Time difference between MA and HTA recommendation.

Results

Marketing Authorisation dates and decisions and HTA dates and recommendations for 16 oncology drug-indication pairs across 4 countries

Average length of time for HTA agencies in England, Scotland, Australia and Canada to publish an HTA recommendation following either MA in Europe, Australia or Canada (left-hand figure), or FDA approval (right-hand figure); FDA approval happened earlier than MA in other countries, with the exception of pembrolizumab in lung cancer and melanoma. The potential time frame from when the drug is in the market (FDA approval), and thus potentially could be accessed by patients, is longer than the amount of time between regulatory approval and HTA recommendation dates in other countries. Additionally, the speed at which pCODR reaches a recommendation becomes less significantly different to the time the other HTA bodies reach a decision when held to the baseline of FDA approval.

Type of evidence submitted to the HTA body for approval, type of economic model used, and pricing arrangements negotiated: Although most HTA bodies received submissions with similar clinical and economic evidence, recommendation outcomes vary greatly.

Cohen's kappa scores measuring inter-rater agreement

Cohen's kappa scores seen were calculated to provide a statistical measure of agreement between the HTA agencies in interpreting the same evidence. Substantial agreement was found between NICE and SMC. None of the other Cohen kappa scores had any agreement between HTA agencies and their respective recommendations across drug-indication pairs. Although kappa values are not as robust as would be preferred, their values highlight the low level of agreement between the various HTA body recommendations.

Conclusions
- Despite the early regulatory approval schemes, HTA agencies do require robust clinical and economic evidence that would allow a positive coverage recommendation.
- However, social value judgements can act as decision modifiers enabling HTA agencies to arrive at positive – mostly restricted - recommendations.

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