VP71 Barriers To Access Biologic Products: A Rapid Review

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Introduction. The elevated costs with biologic products threaten the sustainability of health services, and, therefore, the access to these medicines in the perspectives of user, health professional, health manager and system. The entry of biosimilar products in the market could be an option to subsidize the search for solutions to those problems.

Methods. We conducted a rapid review using the databases Medline (via PubMed), EMBASE, Cochrane Library and CRD. The eligibility criteria were HTAs, systematic reviews and cross-sectional studies.

Results. Literature search retrieved 640 registries and, after duplicate removal, screening of titles and abstracts and full text reading, nine cross-sectional studies were selected. From a user's point of view, the following barriers were identified: lack of knowledge about the medicine, distance between the place of living and the health service (especially in the rural area), long waiting periods for service, passivity in regard to treatment. From a health professional's point of view the barriers were: acceptability of the expert in regard to treatment, interchangeability and substitution, the perception of lack of data showing efficacy and safety. Finally, from the payer's (or health manager) point of view, the barriers were: high cost of medicine, problems with reimbursement and bureaucracy. We did not retrieve any barriers from the health system's perspective from the selected studies.

Conclusions. The entry of biosimilar medicines in the market can induce competition and, therefore, reduce prices of biologic treatments. It is necessary to search for potential solutions to the access barriers identified in this rapid review.

VP72 Impact Of Comparator Choice On Oncology Drugs' Market Access

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Introduction. In France, drug assessment is performed by the Transparency Committee (TC) of the French National Authority for Health (HAS). It's based on two criteria: the clinical benefit (CB) for reimbursement recommendation and the clinical added value (CAV) serving the pricing decision. The CAV is rated on a 5-point scale, from I (major) to V (no CAV). A critical step in the CAV assessment is the identification of the clinically relevant comparators (CRC) serving the TC to recognize the appropriateness of the comparators chosen in the randomized controlled trials (RCT). The objective of this study is to investigate the comparator choice consequences on TC appraisals and pricing.

Methods. A retrospective, descriptive study included all oncology indications assessed by the TC between 2015 and 2017. Based on a pre-specified grid, items on the comparators were extracted from final TC's appraisals.

Results. Among the 135 indications included, the assessed drugs had no CRC in 20% of cases. A RCT was submitted for 89 indications (66%) whose 67 (76%) were conducted versus a CRC. A CRC was identified by the TC for 70% of the 46 indications without RCT. An important/moderate CAV (II-III) was granted when there was a RCT versus a CRC in 70% of cases, versus 50% and 43% for minor (IV) and no CAV respectively. The public price was reduced by 13.5% in average compared to the claimed price without impact of the CAV level (n = 18).

Conclusions. In oncology, comparative data assessed by the TC met its expectations (RCT versus CRC) in a majority of cases. When there is no RCT or a comparison versus a non-relevant comparator the CAV appraisal is decreased. Surprisingly this study hasn't shown any impact of this decrease on the public price. A wider analysis in different medical areas would need to be performed to better investigate these results.

VP74 Orphan Black Box: Explanatory Principles

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Introduction. Orphan legislations over the past thirty years have successfully increased the number of drugs receiving marketing authorization for rare diseases. However, for a therapy to be accessible to most patients, it requires not only marketing authorization, but market access via public reimbursement. In many major markets, the pricing and reimbursement of new therapies is based on an assessment by a national Health Technology Assessment (HTA) body, for which economic value is typically a key consideration. This research evaluates the outcome of HTAs of orphan drugs in Europe.

Methods. HTA decision data (to 31/08/2017) was extracted from Gemeinsame Bundesausschuss (G-BA), Haute Autorité de Santé (HAS), National Institute for Health and Care Excellence (NICE), Pharmaceutical Benefits Advisory Committee (PBAC), and Scottish Medicines Consortium (SMC) websites. EC-approval data was extracted from the European Medicines Agency (to 31/08/2017).

Results. Only a small minority of drugs for orphan diseases received full recommendations for their licensed indication(s) by NICE (3/35, 9%), SMC (8/66, 12%) and PBAC (1/44, 2%). 37% (26/70) of drugs assessed received positive HTA outcome by HAS (ASMR I-III). In Germany, all approved orphan drugs (100/100) received automatic additional benefit post regulatory approval by G-BA.

Conclusions. There have been significant challenges for manufacturers in converting regulatory approval of orphan drugs into commercial success and optimised market access. Attaining positive HTA appraisals for these drugs, which have been approved under expedited regulatory pathways on a less than fully mature

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dataset, whilst also having high prices, due to small patient populations, limiting commercial returns, may necessitate increased utilisation of alternative reimbursement mechanisms.

VP75 Improving Access To Ultra-Orphan Medicines In NHS Scotland

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Introduction. Medicines for very rare conditions present challenges for healthcare globally due to uncertain evidence and often extremely high costs. In 2014, SMC introduced an ultra-orphan framework placing less emphasis on the cost per quality adjusted life year (QALY). Despite this, many medicines continued to be not recommended. A new pathway aimed at improved patient access based on further evidence collection is now being implemented.

Methods. The development of the new pathway has involved collaboration with key stakeholders including patient groups, the pharmaceutical industry, and clinicians. Medicines that meet a new definition (based on four criteria including the prevalence of the condition treated) will be appraised by the SMC committee and a data collection plan will then be agreed with the pharmaceutical company.

Results. From April 2019, medicines validated as ultra-orphans will initially be appraised using the broader decision-making framework and the SMC committee will outline key uncertainties in the clinical effectiveness. The medicine will then be available for a period of at least three years while further data are gathered, potentially comprising ongoing clinical trials, registry data, and patient reported outcome measures. SMC will then re-assess the clinical and economic evidence to inform a final decision on routine use of the medicine in NHS Scotland.

Conclusions. The new pathway for ultra-orphan medicines will allow further evidence on their longer-term clinical benefits to be collected before a final decision on routine use. This approach reflects the current direction of travel in medicines regulation, by making medicines that address an unmet need available to patients at an earlier stage of development.

VP77 Extrapolating ICERs At Different Discount Rates

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Introduction. Applicability of incremental cost-effectiveness ratios from another jurisdiction is often affected by a different local discount rate, creating uncertainty about the ICER using the local discount rate. The ICER is sometimes reported at additional discount rates in the sensitivity analysis. We aimed to investigate the extent to which an ICER can be predicted at a given non-differential discount rate if estimates are available for at least two discount rates.

Methods. We used six previously published economic models representing analyses with a range of time horizons and ICERs calculated at discount rates from 1% to 8%. A simulation exercise was applied whereby the ICER at a discount rate selected from the range 2% to 5% was calculated based on ICERs provided at two or three randomly selected discount rates. With two discount rates a linear model was used to predict the ICER at the selected rate. For three discount rates an exponential model was used. Error between the predicted and actual ICER was calculated as the absolute difference divided by the actual ICER.

Results. For four of the models, ICERs could be well predicted by a linear model (i.e., with two points), with average errors of less than 5%. For the final two models the error was substantial with a linear model but substantially improved to under 15% with an exponential model (i.e., with three data points). The two models with a poor fit to a linear model assessed childhood vaccination programmes over a lifetime horizon.

Conclusions. For studies with a relatively short time-horizon, or where the majority of costs and benefits accrue in the short-term, a simple linear extrapolation can facilitate calculation of the ICER at a discount rate other than those reported. With longer time horizons, a third data point facilitates more reliably extrapolation of ICERs at desired discount rates.

VP82 Impact of Evidence Synthesis Methods on Outcome of Economic Evaluation

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Introduction. Evidence synthesis (ES) is often required for economic evaluation (EE) of pharmaceuticals. Commonly used methods are based on the assumption of proportional hazards in trial data, using the hazard ratio (HR). Alternative methods for ES are increasingly used in EE, in situations where the pattern of hazards in the trial data indicates that the proportional hazards assumption may be violated. The impact of these methodological choices on model outcomes is explored.

Methods. A network of trials of BRAF-targeted treatments for advanced melanoma, derived using a systematic review of the literature, is chosen for the study. Guyot's method is used to create individual-patient Kaplan-Meier (K-M) data from published survival curves. Log-cumulative hazard plots and Schoenfeld residuals are derived to examine patterns in hazards within the trial data. All analyses are conducted in R version 3.5.0©. Three alternative methods for ES are tested: 1) Network meta-analysis (NMA) based on published HRs and the assumption of proportional hazards. 2) NMA using fractional polynomials (FP) based on digitised K-M data, allowing the relaxation of the proportional hazards assumption. 3) NMA using an accelerated failure time (AFT) model based on digitised K-M data, allowing the relaxation of the proportional hazards assumption. The derived estimates of relative efficacy from each method are applied in a partitioned survival cost-effectiveness model programmed in Microsoft Excel™.

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