EUnetHTA WP7: Implementation report November 2018

Appendix – Case study interview summaries

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Health Improvement and Quality Authority (HIQA) - Ireland

Introduction

The Health Improvement and Quality Authority (HIQA) is an independent authority established under the 2007 Health Act in Ireland. HIQA has a broad and wide ranging remit encompassing: setting standards for health and social care services; regulation; monitoring; health information; and **health technology assessment** (HTA).

The HTA directorate at HIQA has a statutory responsibility for evaluating the clinical and cost-effectiveness of health technologies including drugs and to provide advice arising out of the evaluation to the Minister for Health and the Health Service Executive (the body responsible for delivering all of the public health services in Ireland).Although HIQA's responsibility covers all health technologies, the majority of their work to date relates to other technologies (devices and diagnostics) and public health programmes (including vaccines). Appraisal of submissions from manufacturers to inform reimbursement of pharmaceuticals is undertaken by the National Centre for Pharmacoeconomics (NCPE) in Ireland. HIQA is also responsible for the development of national HTA methodological guidelines.

In addition to undertaking HTAs, the HTA directorate at HIQA supports the wider development of HTA capacity and capability through the Irish health service and the incorporation of HTA methodologies into decision-making. It also provides direct technical expertise to support clinical guideline and audit developers meet the quality assurance requirements of national clinical guidelines/audit.

Working practices

HTAs are normally formally requested by the Department of Health (DoH) or Health Service Executive (HSE). The need for a HTA may, however, also be identified through service providers or users, such as a clinical programme or a patient representative group. A prioritisation process is undertaken to ensure HIQA undertakes HTAs that are of maximum benefit to the Irish healthcare system. A prioritisation advisory group, comprising representation from the DOH and HSE formally meets and topics are rated on four areas: clinical impact; (from the perspective of the individual patient and at a population level), economic impact; its relevance in the context of national policy initiatives; and whether or not there is a clear link to decision making for the technology and a reasonable assumption that a HTA could directly contribute to informing the decision-making process. The results of this exercise inform the final HTA work plan.

Chosen topics are subject to a scoping stage which clarifies the research question(s) to be answered. Once terms of reference have been agreed, HIQA appoints an evaluation team from within the HTA directorate to undertake the evaluation. An expert advisory group is also formed, representing all key stakeholder groups. The group normally meets twice face to face during the HTA. Expert advice including access to

data may be also be sought from members at other intervals. On occasion public consultation may be used (normally lasting 6 to 8 weeks), particularly for sensitive or divisive topics.

The HTA report is written by the evaluation team, drafts of which are reviewed and subsequently endorsed by the expert advisory group. A rapid HTA includes a restricted number of domains, but as a minimum includes statements about the clinical effectiveness and safety of the technology. A full HTA includes de novo economic modelling in addition to assessment of the organisational, social and, if relevant, ethical and or legal implications of the technology. The report is submitted as advice to the Minister for Health and HSE and is non-binding. The decision-makers, may also consider other factors when deciding whether to provide the technology. With the exception of pharmaceuticals, there is no stated cost-effectiveness threshold for health technologies in Ireland.

HIQA employ a core team of 6 HTA analysts. HIQA often undertakes complex assessments of multiple technologies. Consequently the time taken to complete assessment can vary, with an average time of 18 months. HIQA normally publishes 2 to 3 assessments per year, although again this can vary depending on the complexity of topics and internal capacity.

Involvement in EUnetHTA and use of assessments

HIQA has been involved in EUnetHTA since the initial EUnetHTA project (2006 to 2008). HIQA has led on the development of a number of tools and methods guides under Work Package 6 and supported the development of others. A number of these have been adapted for use at a national level in Ireland.

HIQA also has been lead / co-author on three EUnetHTA assessments:

- OTCA12 - C-reactive protein point-of-care testing (CRP POCT) to guide antibiotic prescribing in primary care settings for acute respiratory tract infections (RTIs) (JA3 – planned publication date January 2019)

- Endovascular therapy using mechanical thrombectomy devices for acute ischaemic stroke (JA2 - published December 2015)

- Balloon Eustachian tuboplasty for the treatment of Eustachian tube dysfunction (JA2 - published February 2015)

HIQA is / has also been a reviewer on a number of other EUnetHTA assessments including:

- OTCA14 - Robotic surgery in thoracic and visceral indications (JA3 – scheduled to publish February 2019)

- OTCA06 - Transcatheter aortic valve implantation (TAVI) in patients at intermediate surgical risk (JA3 – scheduled to publish December 2018).
- Transcatheter implantable devices for mitral valve repair in adults with chronic mitral valve regurgitation (JA2 – published September 2015)
- Duodenal-jejunal bypass sleeve for the treatment of obesity with or without Type II Diabetes Mellitus (JA2 – published July 2015)
- Prognostic tests for breast cancer recurrence (JA1 – published January 2013))

Benefits of using Joint REA to inform economic evaluation

Joint REAs are particularly useful for defining effectiveness and safety parameters for the economic model, providing a description of the health technology and the burden of disease, and sense-checking of national data / results against EUnetHTA assessments.

In Information provided in the REA regarding the use and reimbursement of the technologies in other countries is useful as it provides important context information for decision makers. It also helps identify agencies / countries that may be able to provide additional information regarding their experience of implementing a technology.

The HIQA scoping process looks at REAs published by EUnetHTA to see if they are applicable to the Irish healthcare system and could be used nationally. The POP database is also reviewed for planned and ongoing work by other agencies to assess opportunities for collaboration or reuse of other work.

Challenges of using Joint REA to inform economic evaluation

Timing is vital, it is difficult to use joint REA if EUnetHTA timelines do not fit with national timelines.

Scoping, the alignment of review questions between EUnetHTA and national work / assessments.

Translation of EUnetHTA joint REA into national documents.

Proposals on how joint REA could be improved for economic evaluation

Include an outline of resource implications in the REA in terms of what is needed to implement the technology.

Clinical effectiveness review could identify cost-effectiveness literature so that national agencies could use this to sense check the data in their models.

National Centre for Pharmacoeconomics (NCPE) – Ireland

Introduction

In Ireland healthcare policy and public health expenditure are governed by the Department of Health (DoH) and administered through the Health Service Executive (HSE). The National Centre for Pharmacoeconomics (NCPE) was founded in 1998 and conducts the health technology assessment (HTA) of pharmaceutical products for the HSE in Ireland.

Following the receipt of an application for reimbursement the Corporate Pharmaceutical Unit (CPU) of the HSE commissions the NCPE to appraise new medicines. The NCPE are commissioned to review the following classes of medicines:

- New active substances seeking reimbursement in Ireland, including those with an orphan designation from the European Medicines Agency
- New indications for currently reimbursed drugs
- Drugs which are already reimbursed by the HSE, and are associated with high expenditure or uncertain clinical benefit.

Working practices

The NCPE employ a two-step process to ensure recommendations are made with expedience and to minimize time to market access for new treatments. All medicines are subjected to a preliminary rapid review. High cost products and those with significant budget impact are subjected to formal economic evaluation. Similarly, products where there is a query in relation to value for money will also be selected for formal economic evaluation.

The rapid review process takes approximately 4 weeks and the formal economic evaluatio0n is completed in less than 3 months. Following assessment, a full appraisal report outlining NCPE conclusions and recommendations is sent to the HSE-CPU to support evidence-based decision-making on reimbursement. The cost-effectiveness threshold for decision-making is currently operating between €20,000/QALY and €45,000/QALY.

The NCPE employ 20 people and undertake approximately 70 rapid review assessments and 20 full HTAs per year.

Involvement in EUnetHTA and use of assessments

The NCPE has been involved in EUnetHTA since Joint Action 2 and is participating as a partner in Joint Action 3. The NCPE was a dedicated reviewer on:

- Sorafenib (Nexavar) the treatment of progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma refractory to radioactive iodine (published March 2015)

The NCPE is a co-author on:

- PTJA04 Sotogliflozin for Type 1 diabetes mellitus (publication date – TBC)

The NCPE used the EUnetHTA assessment on Canagliflozin for the treatment of type 2 diabetes mellitus (published February 2014), making reference to the EUnetHTA assessment in the clinical section. The NCPE also used the EUnetHTA assessment on **z**ostavax for the prevention herpes zoster. The NCPE conducted a review of economic evaluations of zoster vaccine and made reference to the EUnetHTA assessment in the report.

Benefits of using Joint REA to inform economic evaluation

The following information included in joint REAs was identified as being particularly useful / helpful for the purposes of economic evaluation:

- Comparator (if relevant in Irish setting)
- Evidence synthesis
- Treatment effects and how they are applied in the model.
- The main benefit of using joint REA to inform economic evaluation is for the validation of model inputs, in particular long-term epidemiological modelling. The usefulness is directly dependent on timelines and inclusion of relevant comparators.

There have been very few pharmaceutical joint assessments published to date, so it is difficult to for NCPE to comment in detail on the benefits of using EUnetHTA joint REAs. NCPE expect to be able to provide further feedback after use of PTJA03 on alectinib.

Challenges of using Joint REA to inform economic evaluation

Agreement on methodological approaches to evidence synthesis and a process for remaining up to date/responsive to latest developments.

Procedural issues, a decision needs to be made regarding whether fact check will be included as part of the joint assessment process. This is a well-established part of the NCPE process which they consider to be very important, in particular if the assessment ever faces a legal challenge.

Timing of assessments and fitting with national timelines.

Selection of appropriate comparators.

Proposals on how joint REA could be improved for economic evaluation

Include long term clinical modelling. Often the company is extrapolating, so would be good if could use this information to validate the model.

Validation of clinical assumptions, elicitation of clinician opinion of the usefulness of the product/ magnitude of clinical benefit etc.

Information on utility, as above long-term epidemiological modelling using observational evidence. ESMO Magnitude of Clinical Benefit Scale could be useful in addition to GRADE for the clinical evidence for oncology products.

Clinical engagement at an EU level could be very beneficial, in particular for assessment of ultra-orphan drugs where there may be only one clinician in the country with experience of managing a particular condition. EUnetHTA should consider having a pool of people that member states can draw upon.

Consider setting up a Decision Support Unit that would produce up to date guidance on methodological advancements to ensure that best practice is followed in assessments that are produced. Preferably the Unit would be academic and independent.

Scottish Health Technologies Group (SHTG) - Scotland

Introduction

The Scottish Health Technologies Group (SHTG) is part of Healthcare Improvement Scotland (HIS). The remit of SHTG covers non-pharmaceutical health technologies. Pharmaceutical technologies are assessed by the Scottish Medicines Consortium (SMC). SHTG cover all stages of the HTA process, with the exception of decision-making (see below).

Working practices

The majority of topics that SHTG assess come from national or regional health planning committees. Decisions to carry out further work on a topic are made during an evidence review committee (ERC) meeting following an initial work-up by the HIS research team, exploring the topic area, research question and available evidence.

Chosen topics are subject to a scoping stage which clarifies the research question and the most appropriate assessment product. After this the evidence product is produced by the HIS researchers. The ERC then prepare a draft advice statement based on the evidence product. Companies and other stakeholders peer review both the evidence product and advice statement.

The draft advice statement is finalised by the full SHTG, a national scientific committee including representatives from all NHS Scotland territorial health boards, special health boards, academia, industry, the public and HIS research staff. The process from topic referral to production of advice typically takes approximately 6 months.

SHTG employ 10 people and produce between 10 and 15 evidence reviews per year and 2 to 3 innovative medical technology overviews (IMTOs). Both evidence and innovative medical technology overviews include a summary of the clinical and cost effectiveness evidence and include brief consideration of organisational and patient issues.

The status of SHTG advice is ‘required to consider’ and is not mandatory. The advice is disseminated to the 14 NHS Scotland Health Boards. No explicit threshold is applied to decision-making. Committee members are aware of £20-30K threshold, but are not bound by it and can consider other factors.

Involvement in EUnetHTA and use of assessments

SHTG have been involved in EUnetHTA since 2013 (Joint Action 2). SHTG was a reviewer on:

- OTJA08: Continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) as personal, standalone systems in patients with diabetes mellitus treated with insulin (JA3 – published July 2018).

- Transcatheter implantable Devices for mitral valve repair in adults with Chronic Mitral Valve Regurgitation (JA2)

- Endovascular therapy using mechanical thrombectomy devices for acute ischaemic stroke (JA2)

SHTG is currently a reviewer on:

- OTCA12 - The use of C-reactive protein point-of-care testing (CRP POCT) to guide antimicrobial prescribing in primary care settings for respiratory tract infections (RTIs) (JA3 – publication date TBC)

SHTG has adapted three EUnetHTA assessments: transcatheter implantable devices for mitral valve repair; endovascular therapy using mechanical thrombectomy devices and Continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) (OTJA08). The EUnetHTA assessments were adapted to be evidence notes.

The adaptation process has included: condensing the EUnetHTA assessment to fit SHTG evidence note format; removing interventions that were not appropriate to the Scottish context; adding national context information (population size and clinical information); adding health economic evidence (searches for health economic evidence were developed, and the literature reviewed); and updating clinical searches.

Benefits of using Joint REA to inform economic evaluation

Use of joint REAs should definitely free some capacity and resources as no searches and reviewing of the clinical evidence (only adaptation) would be needed. Running searches, reviewing the clinical effectiveness and summarising this takes a lot of time / resource. When this is done as part of EUnetHTA assessment it can save time / resource for economic modelling.

EUnetHTA searches are very good, detailed and systematic.

The following information included in joint REAs was identified as being particularly useful / helpful for economic evaluation and modelling:

- Relative clinical effectiveness data (e.g. survival, reduction in episodes etc.)

- Relative safety data (adverse events)

- Morbidity and quality of life data (e.g. EQ-5D, SF-36)

Challenges of using Joint REA to inform economic evaluation

REA timelines can sometimes not match with national timelines.

Clinical pathways in countries often differ from the trial and the estimate of relative clinical effectiveness may not be applicable.

Proposals on how joint REA could be improved for economic evaluation

Include a detailed description of treatment pathways involved and how the technology assessed fits within the treatment pathway - this would help inform the potential model structure

Including resource use and cost data across various European health systems linked to the technology assessed and comparators would also be valuable. This could be collected as part of a questionnaire that is sent to EUnetHTA partner agencies (or the agencies collaborating in the joint assessment).

Scottish Medicines Consortium (SMC) - Scotland

Introduction

The Scottish Medicines Consortium (SMC) is part of Healthcare Improvement Scotland (HIS). The remit of SMC covers pharmaceuticals. SMC appraises all new medicines and indications licensed by European Medicines Agency (EMA).

Working practices

The SMC is involved in the assessment, appraisal and decision-making stages of HTA, but does not cover scoping. The SMC undertakes single technology appraisals (STAs). It does not currently undertake multiple technology appraisals (MTAs),

SMC undertakes the critical appraisal of company submissions. For each full submission SMC receives, the submitting company must provide an appropriate form of economic evaluation to be critiqued. Each full submission has a pharmacist, health service researcher (HSR) and health economist allocated to work on the critical appraisal; the pharmacist/HSR carries out the critical appraisal of the clinical sections of the company submission and the health economist critiques the economic analysis and budget impact predictions. Clinical and cost-effectiveness issues are reported under separate sections of the SMC advice document, but often issues within the clinical effectiveness will have an impact on the cost-effectiveness. The SMC overall decision is a composite of the clinical and economic case, as well as any wider factors that it felt relevant to its decision-making.

SMC does not have explicit thresholds for decision-making but does reference the £20-30k limits of NICE within its guidance to companies. SMC does not explicitly have different thresholds for different types of medicine, however, SMC does exercise greater flexibility in its decision-making for certain types of treatments through its use of the Patient and Clinician Engagement (PACE) meeting process (i.e. for end of life medicines or medicines to treat rare and very rare conditions).

The recommendations from SMC go to NHS Scotland and is disseminated to the 14 Scottish Health Boards. When SMC accepts a new medicine, NHS boards are expected to make it, or an equivalent SMC-accepted medicine, available. NHS boards publish updated lists of SMC-accepted medicines included and excluded from their formularies together with the reasons for such decisions. As such, SMC recommendations are advisory rather than mandatory, and do not come with specific funding packages for implementation.

SMC employ approximately 35 WTE staff. For the period 2015 to 2017 SMC issued advice for an average of 66 full submissions, 19 abbreviated submissions per annum.

Involvement in EUnetHTA and use of assessments

SMC have been participating in EUnetHTA since Joint Action 2 (JA2). SMC was a reviewer on the following assessments under JA2:

- Vorapaxar for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infection (MI) (published June 2015)
- Sorafenib for the treatment of progressive, locally advance or metastatic, differentiated (papillary/follicular/hurthle cell) thyroid carcinoma, refractory to radioactive iodin (published March 2015)
- New pharmaceuticals for the treatment of chronic hepatitis C (published December 2015)

Under Joint Action 3 (JA3) SMC has observer status on:

- PTJA04 - Sotagliflozin for Type 1 diabetes mellitus (publication date – TBC)

And reviewer status on:

- PTJA05 - Enasidenib for the treatment of adult patients with relapsed or refractory acute myeloid leukaemia (AML) with an isocitrate dehydrogenase 2 (IDH2) mutation (publication date – TBC)

To date SMC has used EUnetHTA joint REAs for clinical assessment only. SMC have used the three published JA3 pharma assessments (midostaurin, regorafenib, alectinib) to validate data from the company submissions to SMC. The JA2 assessments were identified as being less useful because of timing (availability was too late to contribute to SMC assessment).

Benefits of using Joint REA to inform economic evaluation

The main benefits of using joint REAs to inform economic evaluation were: more efficient use of resources/ to help validate and provide reassurance and sense-checks of individual country HTA economic assessments; increased confidence in results when using EUnetHTA assessments; and indirect treatment comparisons.

The information in joint REAs identified as being most useful for the purposes of economic evaluation is relative effectiveness data versus relevant comparators.

Challenges of using Joint REA to inform economic evaluation

Applicability of joint REA to Scottish practice, e.g. relevant comparator, resource use/ patterns of care differing between countries

Timelines are very tight in Scotland with reviewers typically taking 4 to 5 weeks to undertake the assessment of company's submission and 18 to 22 weeks from receipt of company's submission to publication of advice.

Processes - current SMC HTA process starts with company's submission.

Proposals on how joint REA could be improved for economic evaluation
Difficult to comment as only had 3 pharmaceutical assessments under JA3.

Scoping work to establish the main comparators across EU for use in the REA and the potential use of several different comparator options to accommodate most frequently used treatments. Alternatively, the assessments could focus on those areas where a high degree of consistency is known to exist in treatment patterns across the relevant nations.

When head to head studies are not available, indirect comparisons versus relevant comparators in countries would be useful.

Health Technology Wales (HTW) – Wales

Introduction

Health Technology Wales (HTW) was established by the Welsh Government in November 2017 as an independent, national body that collaborates with NHS Wales and partners to identify, appraise and offer guidance on high impact non medicine care technologies. The remit of HTW covers all non-pharmaceutical technologies (including medical devices, surgical procedures and tele-monitoring).

Working practices

The work of HTW is covers three principal areas as described below. Unlike many HTA agencies HTW Also has a role in the adoption of health technologies.

- Identification (including horizon scanning) - HTW collaborates with partners across the health, social care and technology sectors to ensure a consistent, national approach to the identification of technologies expected to have a major impact on future health and care in Wales. HTW also signposts technology innovators to the relevant organisations within Wales who can provide advice and support.
- Appraisal - HTW independently assesses non-medicine healthcare technologies and issue independent guidance based on the best available evidence and expertise. HTW's work aims to inform commissioning by NHS Wales and care providers and supports decision makers to make evidence-informed decisions on both technology investments and disinvestments.
- Adoption - HTW monitors the uptake of HTW advice and advice from other organisations e.g. NICE across the Welsh health boards. This includes both adoption of new technologies and disinvestment of older, less effective technologies.

Advice from HTW is disseminated to NHS Wales and the 7 local health boards in Wales. The Advice is not mandatory, but the working practice is to 'adopt or justify' meaning a rationale / reason must be given for any advice not adopted.

There is no formal cost-effectiveness threshold, but HTW look to work in line with the NICE threshold of £20,000 to £30,000 per QALY. HTW employ 17 staff and plan to undertake 15 to 20 rapid reviews per year, though this number may be revised down if full HTAs are undertaken.

Involvement in EUnetHTA and use of assessments

HTW was established too late to join Joint Action 3 (JA3). HTW have been linking in with JA3 through the All Wales Therapeutics and Technology Centre (AWTTC). Furthermore, the Director of HTW (Susan Myles) has been previously involved in EUnetHTA through her previous role at Health Improvement Scotland (HIS).

Under JA3 HTW was a reviewer on:

OTJA08 - Continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) as personal, standalone systems in patients with diabetes mellitus treated with insulin (published July 2018)

HTW used OTJA08 as a reference check for their national assessment. The use of the assessment was limited by delays to the publication of EUnetHTA assessment, which meant that the HTW assessment was completed before the EUnetHTA assessment OTJAA08 was published.

Benefits of using Joint REA to inform economic evaluation

Joint REAs provide information on key outcomes, data and parameters for the economic model

Joint REAs offer significant potential to reduce duplication, saving time and resources.

Challenges of using Joint REA to inform economic evaluation

Timeliness and fitting with HTW timelines.

Practicalities of accessing the model where there is confidential data, obtaining the model and having the time to understand it locally.

Methods to be applied when using the REA and undertaking economic evaluation – methods guides from EUnetHTA are very helpful

Proposals on how joint REA could be improved for economic evaluation

More collaboration, more quickly and more often and less duplication.

Consider including economic model in the joint assessment alongside the clinical assessment (full HTA).

Provide information within the joint REA on key areas / issues to be considered in the economic model – based on the findings from the clinical effectiveness review.

Guidance on intellectual property for models as addressing this issue is often very time consuming.

Zorginstituut Nederland (ZIN) - Netherlands

Introduction

ZIN undertakes a number of tasks associated with healthcare in the Netherlands, including HTA. Under Dutch legislation for a health technology to be reimbursed it must be of comparable effectiveness or greater effectiveness than the existing treatment. ZIN produces health technology assessments to inform decisions about the reimbursement status of pharmaceutical and non-pharmaceutical medical technologies (medical devices, hospital interventions or non-hospital/outpatient interventions).

The largest number of assessments produced by ZIN are for non-hospital pharmaceutical technologies. ZIN does not have to carry out assessments of all pharmaceutical technologies and does not assess generic pharmaceuticals.

Working practices

For outpatient pharmaceuticals the company applies for reimbursement, for inpatient pharmaceuticals ZIN selects technologies for assessment and plans activity. For non-pharmaceutical health technologies requests for assessment can be received from a range of stakeholders.

The pharmaceutical assessment procedure usually starts after the marketing authorisation. Once the company submission is received ZIN prepares an assessment using evidence from the application and other sources to assess the technology. ZIN have 70 days (outpatient drugs) to prepare advice for the Ministry. The Ministry then has 20 days to make a final decision. The 70 days represents approximately 1 month to write a draft report that is then scheduled into a monthly Scientific Committee meeting for discussion before being amended. The assessment will then go through a stakeholder review before being reviewed again by the Scientific Committee. The management board of ZIN then issues advice to the Ministry of Health about the use of a technology and whether price negotiations should take place. ZIN does not take part in price negotiations, these are taken forward by the Ministry of Health.

For other technologies ZIN make recommendations to health insurers. The advice should be and generally is followed.

ZIN does not have a specific threshold for decision-making but does operate a reference value that depends on the severity of the burden of disease calculated using proportional shortfall – based on 3 reference values. Higher disease burden means a proportionality higher ICER being accepted ranging from €80,000 Euros per QALY (upper value), middle value is €50k Euros per QALY and lower value is €20k Euros per QALY.

ZIN employ approximately 300 people in total, with about 60 working on HTA. ZIN produce 50 to 60 assessments per year (including pharma and other technology assessments).

Involvement in EUnetHTA and use of assessments

ZIN has been involved in EUnetHTA since the start of the first EUnetHTA project in 2006.

Under JA3 ZIN was lead author on:

- OTCA04 - MammaPrint – Added value of using the gene expression signature test MammaPrint for adjuvant chemotherapy decision-making in early breast cancer (published January 2018).

Under JA3 ZIN is a co-author on

- PTJA04 - Sotagliflozin for Type 1 diabetes mellitus (publication date TBC).

Under JA3 ZIN was a reviewer on:

- PTJA01 - Midostaurin in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy (published November 2017).

ZIN also participated in a number of assessments under Joint Action 2.

For OTCA04 (Mammaprint) ZIN planned to use the assessment to do a collaborative economic evaluation with Belgium. However, the conclusion of the clinical effectiveness assessment was that it was not effective so this prevented the economic evaluation from proceeding.

The use other EUnetHTA joint assessments by ZIN has been limited by the EUnetHTA assessment not being available at the time national work was being undertaken or because the product was not assessed in the Netherlands.

Benefits of using Joint REA to inform economic evaluation

A well undertaken REA that you can trust gives you the core information and 'engine' for your economic model and also good information for long term extrapolations.

The REA gives HTA assessors at a national level confidence because they know it has been developed and reviewed at a European level and the clinical effectiveness review will have been taken to a high quality. Joint REAs are very useful as a trusted opinion source that can be used to check / validate national work.

Joint REA also gives good information on outcome measures, quality of life and treatment side effects.

When undertaking economic evaluation you often have to await for clinical effectiveness analysis, so can use joint REAs in these instances to inform data for the economic model.

It would be great to could have lots of European REAs that could be plugged into economic models at a national level,

Challenges of using Joint REA to inform economic evaluation

Not all joint REAs produced are relevant as the Netherlands do not assess all pharmaceuticals and the EUnetHTA assessment may not be relevant / applicable to the Dutch context.

Need to be clear that joint REA is / will be finished before national work is commenced.

Key issue preventing use of joint REAs is if the REA uses different outcomes and comparators than is expected to be used in the economic evaluation and model.

Also language can be a challenge / issue because reports have to be translated into Dutch language due to current legislation.

Proposals on how joint REA could be improved for economic evaluation

Increased availability of joint REAs for use in economic modelling.

Improved presentation and consistency of information - the presentation of information is often different in joint REAs and this creates issues because you then have different data for the economic model.

More information on quality of life and quality of life instruments in joint REAs would be useful.

Treatment pathways and models of care are different between countries, so information on this would be helpful also.

The National Institute of Pharmacy and Nutrition (NIPN) – Hungary

Introduction

The HTA Department in the National Institute of Pharmacy and Nutrition (NIPN) produces reports that are used by the National Health Insurance Fund (NHIF) and Ministry of Human Capacities to make decisions about national reimbursement and pricing of pharmaceuticals and other health technologies in Hungary.

Working practices

For all technologies, companies submit for reimbursement to the National Health Insurance Fund (NHIF) who forwards the submission to NIPN for review. Companies can submit for reimbursement in Hungary following receipt of marketing authorisation once a product is reimbursed in 3 other European countries.

NIPN reviews the evidence submitted and provides a report to NHIF. In their review, NIPN will check the appropriateness and robustness of the company's submission including the appropriateness of the proposed place in therapy, appropriateness of the included clinical evidence and a critical evaluation of the health economic evaluation (not for medical aids) and budget impact analysis. The consistency of the clinical data with the cost effectiveness modelling will also be checked.

The reports for medical devices contain a recommendation on the reimbursement of the technology. These reports are then sent back to NHIF who hosts the meetings of the Technology Assessment Committee. The final recommendation is made by the Technology Assessment Committee that includes representatives of NHIF, clinicians, the Ministry of Human Capacities and NIPN.

NIPN employ 15 people. The HTA Department produces approximately 200 outputs per year including 90-100 pharmaceutical reports, 90-100 reports about medical aids used by patients and 4-5 healthcare technology reports about medical devices used by physicians in hospitals. The pharmaceutical and healthcare technology reports include a review of the company's submitted evidence of clinical effectiveness, cost-effectiveness and budget impact, the reports for medical aids include a clinical overview and assessment of budget impact comparing the prices and attributes of the devices.

Involvement in EUnetHTA and use of assessments

NIPN began participating in EUnetHTA in 2010 under Joint Action 1 (JA1).

Under JA3 NIPN is a dedicated reviewer for:

- OTCA02 - Antibacterial-coated Sutures Versus Non-Antibacterial-Coated Sutures for the Prevention of Abdominal, Superficial and Deep Incisional, Surgical Site Infection (SSI) (published April 2017).
- OTCA03 – Screening of fetal trisomies 21, 18 and 13 by non invasive prenatal testing (published February 2018).
- OTCA 11 - The use of 3D printing for implants and splints in connection with surgery (publication date – TBC).
- OTCA 15 - Irreversible electroporation in liver and pancreatic cancer (to be published May 2019).
- PTJA02 - Regorafenib indicated as monotherapy for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib (published October 2010).
- PTJA03 - Alectinib as monotherapy for the first line treatment of adult patients with ALK-positive advanced non-small cell lung cancer (NSCLC) (published January 2018).

In their national procedures NIPN used the EUnetHTA reports for canagliflozin for the treatment of type 2 diabetes mellitus and ramucirumab in combination with paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction adenocarcinoma to support their national assessments. NIPN used the Alectinib assessment (PTJA03) to sense check their national assessment.

NIPN review company submissions rather than produce HTAs. NIPN have, therefore, generally used EUnetHTA assessments and specifically the relative effectiveness data as a source of information in the clinical effectiveness section of their report to support their review of the company submission and check the comparability of the data submitted.

Benefits of using Joint REA to inform economic evaluation

EUnetHTA assessments give validity and credibility to national work, enabling member states to draw on findings from EU wide work undertaken to a high quality. EUnetHTA assessments can also save time / effort in reviewing other agencies evaluations and save time on reading additional literature and looking for evidence.

The information on end points provided in joint REAs is identified as particularly important and useful for national assessments.

Challenges of using Joint REA to inform economic evaluation

The biggest challenge is timing as often national assessments and economic modelling need to have been completed before the EUnetHTA assessments starts or is completed. For this reason EUnetHTA assessments have principally been used by NIPN to check clinical data and sense check national assessments.

Proposals on how joint REA could be improved for economic evaluation

Industry representatives from bigger EU markets are familiar with and clear on the purpose of EUnetHTA assessments. However, in smaller markets industry representatives are not familiar with EUnetHTA assessments. Better dissemination and communication is needed with these smaller markets and countries to make them aware of EUnetHTA, how it works and the joint assessments that EUnetHTA produces.

It was suggested that the information in joint REAs could be improved by providing information on sub-group analysis for comparators and also through providing some information on the dose of each compound in the assessment of pharmaceuticals

The Norwegian Medicines Agency (NOMA) – Norway

Introduction

The Norwegian Medicines Agency (NOMA) is the national agency responsible for HTA of pharmaceuticals in Norway. NOMA undertake assessment of relative-effectiveness compare to existing therapy and cost-effectiveness is mandatory for all new drugs. NOMA mainly undertake a critical appraisal of single technology HTA provided by the pharmaceutical company in their submission file. NOMA does not perform independent analysis.

Working practices

The submission for reimbursement of out-patient drugs is voluntary in Norway. The pharmaceutical company decide whether they wish to apply for reimbursement.

For in-patient drugs there is a topic selection based on list of new-drugs and new indications published by EMA. All new drugs for in-patient use have to be assessed before a decision for public financing.

NOMA is responsible for the process of reimbursement of out-patients drugs (HTA + decision-making). For in-patients drugs the process is different. NOMA still does a critical appraisal of submission files from pharmaceutical companies, but are not the decision-maker. The decision for public reimbursement is made by the hospitals and is partially based on the NOMA recommendation.

There are no public explicit thresholds for decision-making. Willingness to pay per QALY gained is dependent on severity of the disease (measured as absolute shortfall of QALYs). Budget impact and uncertainty in the documentation of incremental costs per QALYs are potential modifiers. The higher the absolute shortfall, the higher WTP per QALY gained.

NOMA employs approximately 300 people in total and 30 person years is allocated to the HTA unit. NOMA produces approximately 40 assessments of in-patients pharmaceuticals and approximately 15-20 for out-patients pharmaceuticals per year.

Involvement in EUnetHTA and use of assessments

NOMA has been participating in EUnetHTA since May 2016 (Joint Action 3). NOMA was co-author for the joint assessment on:

- PTJA01 - Midostaurin with standard chemotherapy in FLT3-positive acute myeloid leukaemia (published November 2017)

NOMA used the published results from the Regorafenib (PTJA02) and Alectininb (PTJA03) joint assessments. The joint assessments were mainly used for clinical assessments of relative-effectiveness (point-estimates) and for discussions for choice of relevant comparator/ alternative therapies.

Benefits of using Joint REA to inform economic evaluation

- Identification of all relevant comparators.
- Reliably of results from literature search.
- Point estimates of relative-effectiveness.

Challenges of using Joint REA to inform economic evaluation

- Methodological and procedural issues,
- Timeliness of joint assessments and fit with national timelines.
- Limited number of joint REAs available.

Proposals on how joint REA could be improved for economic evaluation

Substantial increase in the number of joint REAs produced in the near future.

Close cooperation with end-user (decision-makers and payers) to make sure that the final product is fit for purpose.

Content: Less general information about the disease and all possible treatments. More focused report directly on REA and based on relevant comparators.

Inclusion of different type of studies and unpublished data to make the report more up-to date. The company would then use updated data in the economic analysis.

Extrapolation of results beyond study period.

Identification of all relevant resources.

The Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) – Sweden

Introduction

The Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) was founded in 1987 and is one of the oldest HTA agencies in the world. The remit of SBU covers pharmaceuticals and other technologies (TLV in Sweden also assess pharmaceuticals). Originally the remit of SBU covered health technologies only, but this has now been expanded to include social services interventions as well.

Working practices

HTA topics can be suggested by health and social care professionals, patients, the Swedish government, other national agencies and by SBU themselves. Prioritisation of topics is based on 10 agreed prioritisation criteria. SBU are involved in scoping, assessment and appraisal, but not decision-making. For health technologies decision-making is regional and is made by 21 regional health authorities. SBU disseminates evidence to the decision-makers.

Economic modelling is accepted by SBU, and the type of model is dependent on specific decision problem. Cost-utility analysis (CUA) is preferred by SBU, though cost-consequence analysis is sometimes undertaken. Budget impact analysis is also undertaken by SBU.

SBU has circa 80 employees in total and produces approximately 12 full HTAs per year – plus a range of other products. The time taken to complete a full HTA varies based on complexity, on average taking 2 to 3 years for each assessment.

Involvement in EUnetHTA and use of assessments

SBU began participating in EUnetHTA under Joint Action 1 (JA1). SBU has not been involved in any EUnetHTA joint assessments, either as an author or reviewer. SBU, has, however, been involved in developing the EUnetHTA core model and various EUnetHTA methods guides.

SBU has not adapted any EUnetHTA assessments for use at a national level, with the exception of the joint EUnetHTA report on Screening for Abdominal Aorta Aneurysm (AAA) in a national uptake, published in November 2015 and January 2016.

The principal reason for not using joint assessments relates to timing, with EUnetHTA joint assessments often not available or complete at the time of national assessments.

Benefits of using Joint REA to inform economic evaluation

Difficult to comment as not been involved in producing or using EUnetHTA joint assessments. Biggest anticipated benefits are significant savings in time and resources and reduction in duplication.

Challenges of using Joint REA to inform economic evaluation

A lack of time between having the evidence on clinical evidence and then using this evidence to undertake a good cost-effectiveness analysis. The biggest challenge is having the time to do a good health economic analysis based on the clinical evidence.

Methods used in joint assessments and quality issues as well as compliance with HTA standards

Access to data and confidentiality of data.

Requires that the assessments would include a PICO, mainly subpopulation and outcomes that are of interest to the Swedish context.

Methodologies employed and data sources used need to be very clearly described for transparency and quality assessment.

Proposals on how joint REA could be improved for economic evaluation

Clear reporting of data and the possibility to make adjustments to make the data applicable to different contexts, settings and countries.

Methods for undertaking joint REAs should be very transparent to make agencies more willing / confident to use joint assessments. SBU would need to be assured of the methodological quality before they could / would consider using the joint assessments.