EUnetHTA WP7: Implementation report May 2019

Appendix – Case study interview summaries

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AETS-ISCIII – Spain

Introduction

Health Technology Assessment Agency (AETS) is a National Agency founded in 1994 as a Centre within the Institute of Health Carlos III (ISCIII). ISCIII is the main Public Research Entity funding, managing and carrying out biomedical research in Spain reporting to Ministry of Economy, Industry & Competitiveness and providing scientific and technical support to the Ministry of Health and to the National Health System (NHS).

The main goal of the AETS-ISCIII is to promote the appropriate use of health technologies, providing decision-makers with critically review information about their efficacy, safety, effectiveness and efficiency.

Working practices

AETS-ISCIII is a producer of HTA and has a national remit. AETS mainly undertakes HTA of other technologies. AETS undertake both single and multiple technology appraisals. Economic evaluation is not undertaken as standard for all topics, the decision on whether to undertake economic evaluation is dependent on the topic. Topics are referred to AETS by the Spanish HTA Network. As a member of the Spanish HTA Network, AETS-ISCIII has a role in topic selection, scoping and assessment. The agency has no role in decision-making.

The Spanish Network of HTA Agencies is a collaboration of eight HTA agencies working together to produce national HTA of non-pharmaceutical medical technologies in Spain. The reports produced by the Spanish Network are commissioned and funded by the Spanish Ministry of Health.

Involvement in developing EUnetHTA tools and methodology guidelines

AETS-ISCIII was involved in the development of the HTA Core Model and the EVIDENT database. The agency was also a reviewer on the POP database and some of the methodological guidelines, including:

- Endpoints used in REA: Safety
- Therapeutic medical devices

The involvement of the agency in developing and reviewing guidelines was helpful in developing and updating national guidelines as EUnetHTA tools and guidelines were used inform this process.

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Use of EUnetHTA tools and methodology guidelines

The HTA Core Model has been used as a basis for national reports and a guideline based on the HTA Core Model was elaborated and officially approved for use by the Spanish HTA Network. In 2016 Spanish HTA Network published national guideline for rapid REAs based on the HTA Core Model and the 4 domains of the model. A consultation on this was undertaken by all of the agencies in the Spanish HTA Network, with no legal changes were required. Minor changes were made to the HTA Core Model in the process of national adaptation, mainly synthesis of assessment elements and translation into Spanish.

The POP Database is used by AETSC-ISCIIII to search for other projects and to notify other agencies of planned and ongoing projects they are undertaking.

A number of the EUnetHTA methodology guidelines are used by AETS-ISCIII as methodological references guides for the elaboration of HTA reports. Where AETS-ISCIII have not used EUnetHTA methodology guidelines this has been because they have not been needed, rather than because an explicit decision has been taken to use the guideline(s).

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

AETS-ISCIII did not identify any of the EUnetHTA methodology guidelines as limiting their ability to use EUnetHTA assessments. The following EUnetHTA guidelines were identified as specifically supporting their use of EUnetHTA assessments:

- Process of information retrieval for systematic reviews and HTAs on clinical effectiveness
- Endpoints used for REA: Clinical endpoints
- Endpoints used for REA: Health-related quality of life and utility measures
- Endpoints used for REA: Safety
- Levels of evidence – Applicability of evidence for the context of a REA
- Methods for health economic evaluation
- Internal validity of non-randomised controlled studies (NRS) on interventions
- Therapeutic medical services
- Personalised medicine and co-dependent technologies

In the case of the therapeutic medical services guideline AETS-ISCII report that this is an area where there is not much methodological guidance, so this guideline is important because it provides a methodological framework for this topic / area.

AETS-ISCIII identified that if methodological guidelines focus on the discussion of methods and they do not provide you with practical recommendations or specific points of action then different agencies could interpret and use the methods guidelines in different ways. This may in turn impact on uptake in the future after JA3.

Priority areas for improvement in EUnetHTA guidelines and methods development

Guidelines could be more definitive / prescriptive in terms of how to apply methods. The guidelines need to better describe how to undertake an assessment, not provide a discussion on methods to be used.

Complex interventions: Interventions other than devices and pharmaceutical products are difficult to assess and a guideline, protocol, standard, or methodology would be helpful. The agency is seeing an increasing demand to assess complex interventions that are often part of complex care pathways.

A tool on CE marking (sources to obtain information).

POP database is currently underused. Clarity is also needed on the future status of the EVIDENT database.

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DEFACTUM - Denmark

Introduction

DEFACTUM is a regional organization undertaking evaluation, quality improvement and research within healthcare, social services and the labour market. DEFACTUM is a part of Corporate Quality in Central Denmark Region.

Public Health & Health Services Research is a division in DEFACTUM with focus on research within health care and social services. One of their main tasks is to support decision-makers on interventions and technology within healthcare based on interdisciplinary research and development activities. One of the ways they do this is by producing health technology assessments of medical interventions and health technologies (other technologies).

Working practices

DEFACTUM has a national and regional remit. They produce mainly national reports, but also produce regional reports on occasion. DEFACTUM mainly undertake multiple technology appraisals. Economic evaluation is undertaken standard as part the HTA process. DEFACTUM also undertake organisational analysis as standard in their HTA as well as patient perspective analysis if relevant.

Topics are agreed by the health directors of the five regions. DEFACTUM undertakes the assessment and draw up conclusions. This then goes to the decision-makers (the health directors of the five regions) to make the final recommendations and decision on the technology and use of the HTA report. The health directors also distribute the report to relevant clinicians.

Involvement in developing EUnetHTA tools and methodology guidelines

DEFACTUM were part of the team that developed and specified the patient and social aspects of the EUnetHTA HTA Core Model. DEFACTUM was also involved in the development of the organisational aspect of the HTA Core Model. DEFACTUM has not been involved in the development of any other EUnetHTA tools or methodology guidelines. DEFACTUM has, however, also participated in the formal consultations on draft tools and methodology guidelines.

DEFACTUM has largely been involved in the development of several joint assessments, as first author, co-authors and dedicated reviewers. They have also used several the EUnetHTA joint REA assessments nationally.

Use of EUnetHTA tools and methodology guidelines

POP database: Enter topics into the database and check the database before undertaking an assessment.

HTA Core Model and REA Model: Use the HTA core model to undertake national assessments and the use of the HTA Core Model is now embedded into national methods and processes. HTA core model and REA incorporated through adaptation of the HTA core model nationally. Main challenge was the need to translate into Danish language.

Evidence submission template: Used when undertaking national HTAs. They use a shortened version of the submission template nationally (one third of a size of the EUnetHTA shortened version). The template is identified as being extremely useful for both DEFACTUM and the companies using it.

DEFACTUM also use various methods guides informally on an as needed basis:

- Process of information retrieval – informal use (very rarely used as have own processes)
- Endpoints used for REA assessment: clinical endpoints
- Endpoints used for REA assessment HRQoL and utility measures
- Endpoints used for REA assessment: safety: informal use
- Endpoints used for REA assessment: composite endpoints
- Endpoints used for REA assessment: surrogate endpoints

DEFACTUM have not specifically decided not to use the other EUnetHTA methodology guidelines. They have not needed to use these EUnetHTA methodology guidelines because they already have established methods in many of these areas.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

No methodology guidelines were identified in the online survey as specifically supporting or limiting use of EUnetHTA assessments.

Priority areas for improvement in EUnetHTA guidelines and methods development

Guidelines are very thorough so not much needs to be added.

Guidance on how to undertake organisational analysis would be helpful as would further guidance on economic evaluation. Also consider expansion the REA model expanded to include organisational aspects / elements.

IQWiG - Germany

Introduction

The Institute for Quality and Efficiency in Health Care (IQWIG) was established in 2004. The Institute produces independent, evidence-based reports on:

- drugs
- non-drug interventions (e.g. surgical procedures)
- diagnostic tests and screening tests
- clinical practice guidelines (CPGs) and disease management programmes (DMPs)

Working practices

IQWiG is a producer of HTA with a national remit that covers both pharmaceuticals and other technologies. IQWiG undertake both single and multiple technology appraisals. IQWIG do not undertake cost-effectiveness analysis, they undertake cost analysis only (a limited form of budget impact).

Topics are commissioned by G-BA or Ministry of Health. IQWiG are involved in setting the scope for the assessment (e.g. defining outcomes) and undertake the assessment. IQWiG then make a recommendation. Decision-maker is G-BA.

IQWiG methods are described in a publicly available methods manual: https://www.iqwig.de/download/Allgemeine-Methoden_Version-5-0.pdf

Involvement in developing EUnetHTA tools and methodology guidelines

IQWiG has been involved in the development of 11 different EUnetHTA tools and guidelines as a developer, author or reviewer:

Companion Guide - Developer

Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness” – Developer

Guideline “Endpoints used in REA of pharmaceuticals: Composite endpoints” - Developer

Guideline “Endpoints used in REA of pharmaceuticals: Safety” -Developer of adapted version

Guideline “Levels of evidence: Internal validity of randomized controlled trials” – Developer

Guideline “Internal validity of non-randomised studies (NRS) on interventions” – Developer

Guideline “Meta-analysis of Diagnostic Test Accuracy Studies” – Co-author

Guideline “Therapeutic medical devices” - Co-author

Reflection paper on “Personalised medicine and co-dependent technologies” – Developer

Guideline “Methods for health economic evaluations” – Co-author

Guideline “Critical assessment of clinical evidence” (under development) - Developer

Guideline “Critical assessment of economic evaluations” (under development) - Reviewer

Use of EUnetHTA tools and methodology guidelines

POP database – continuously updating IQWIG planned and ongoing projects in the POP database and also use the POP database as an optional source for the identification of current research activities in preliminary searches.

HTA adaptation toolkit – use an adapted form of the checklist for the evaluation of the transferability of results from systematic reviews of economic evaluations within the ‘ThemenCheck Medizin’ (an HTA procedure based on topics suggested by the general public). Used only selected items of the checklist and some items were rephrased. Translated into German to be applicable to German context.

Process of information retrieval for systematic reviews and HTAs on clinical effectiveness – cited and referred to by the information retrieval department at IQWiG.

Do not need to use or consider using a number of the EUnetHTA guidelines as IQWiG has established national methods that are defined in methods manual that pre-date EUnetHTA methods guidelines. There are also some aspects included in guidelines and tools that might preclude IQWiG using them in the future, for example in the safety guideline the presentation of how evidence from observational evidence might be used deviates from their own agency requirements.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

For pharmaceuticals IQWiG cannot use the EUnetHTA assessments for legal reasons and as a consequence the EUnetHTA guidelines cannot have an impact on uptake of EUnetHTA assessments. For other technologies some contents of guidelines support use of EUnetHTA assessments and some limit.

LBI HTA – Austria

Introduction

The Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA) is an independent academic institute providing scientific decision-making support in the health sector. The institute is funded by the Ludwig Boltzmann Society (40%), The Ministry of Health, Federation of Social Insurers and Regional Health funds (together 60%). It works across a number of research areas covering a wide range of health technologies including high-tech medical devices, interventional procedures, oncology medicines, screening and prevention, rehabilitation and psychology. LBI-HTA was established in 2006 and publishes approximately 22 outputs each year including HTAs, decision support documents for the hospital benefit catalogue and horizon scanning in oncology documents.

Working practices

The process of identifying topics and timelines for producing HTA varies depending on the research area and output. For the evaluation of new high-tech interventions in hospitals, topics are proposed annually by stakeholders (such as hospitals or specialist clinicians) for inclusion in the benefit catalogue. Proposals are collected by the Ministry of Health and priorities are set and approved by the Federal Health Commission. Based on the final selection of topics LBI-HTA produces HTA for each of these topics. The HTA reports and recommendations produced by LBI-HTA are appraised and discussed by a committee of regional representatives of payers before a final decision on reimbursement and coverage is made by the Federal Health Commission. The procedure is carried out to strict timelines where HTA is completed from November to March each year. LBI-HTA produce their own reports and also adapt HTAs produced by other agencies or EUnetHTA.

Involvement in developing EUnetHTA tools and methodology guidelines

LBI-HTA has been a member of EUnetHTA since the first joint action starting in 2010. LBI-HTA was involved in the development of the POP database and they still undertake the maintenance of the POP database.

Use of EUnetHTA tools and methodology guidelines

LBI-HTA use all the EUnetHTA tools and guidelines apart from the EVIDENT database and the EUnetHTA guideline on methods for health economic evaluation. The EVIDENT database is currently offline and LBI-HTA do not have reason to use the EUnetHTA health economic guideline as they do not undertake economic evaluation. Examples of how LBI-HTA use EUnetHTA tools and methodology guidelines include:

POP database: When topics are commissioned by the Ministry of Health, LBI-HTA check the POP database for overlaps. They also enter their own topics into the database.

HTA Core Model: LBI-HTA adapted national assessment template to have the same structure (including the research questions) as the EUnetHTA assessment template. The LBI-HTA methods manual published in 2012 references the HTA Core Model.

Evidence submission template: This is only used by LBI-HTA when conducting EUnetHTA assessments.

Methodological guides: The EUnetHTA methodology guidelines are used formally and are incorporated into the assessment template that LB-HTA use. It is highlighted that authors should consult EUnetHTA guidelines (with links to the guidelines provided).

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

LBI-HTA report that they view EUnetHTA assessments as being of high quality. LBI-HTA generally look to use EUnetHTA assessments if they are referred a topic that has been subject to a EUnetHTA assessment. All the EUnetHTA methodology guidelines were identified by LBIHTA as *significantly supporting* their use of EUnetHTA assessments. No guidelines were identified as limiting use.

Priority areas for improvement in EUnetHTA guidelines and methods development

EUnetHTA Guideline on critical assessment of clinical evaluations is currently in development and will be helpful for all partners as this will help to ensure high quality of assessments.

Use of GRADE as standard EUnetHTA practice would improve uptake as LBI use GRADE nationally. Where a EUnetHTA assessment does not use GRADE, then LBI have to undertake further work grading evidence when using the EUnetHTA assessment nationally.

Real world evidence – this is an emerging area for many HTA agencies.

Guidance is required and would be helpful on HTA methods for orphan diseases.

It was also proposed that EUnetHTA methodology guidelines need to be regularly reviewed and updated.

It was also suggested that EUnetHTA should simplify and shorten the EUnetHTA evidence submission template.

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 compared to existing therapies. 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 key role of NoMA is producing HTA for both primary care ("out-patients") and specialist care ("in-patients"). The submission for reimbursement of out-patient drugs is voluntary in Norway. The pharmaceutical company decide whether they wish to apply for reimbursement but if they do so they have to submit HTA documentation. The basic requirements are the same. For in-patient drugs there is a topic identification based on list of new-drugs and new indications published by EMA. All new drugs for in-patient use must be assessed before a decision for public financing.

NoMA is responsible for the whole process of reimbursement of out-patient 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.

NoMA produces approximately 40 assessments of inpatient pharmaceuticals and approximately 15-20 for out-patients pharmaceuticals per year.

Involvement in developing EUnetHTA tools and methodology guidelines

NOMA has been participating in EUnetHTA since May 2016 (JA3). NoMA has not been involved in the development of any EUnetHTA tools and methodology guidelines. NOMA was, however, a co-author for the EUnetHTA joint REA assessment on Midostaurin (PTJA01).

Use of EUnetHTA tools and methodology guidelines

NoMA report that they have not directly used any of the EunetHTA tools and guidelines in national procedures. These is mainly because the agency already has existing national guidelines and methods that they work to. There is also a view that EunetHTA methodology guidelines are often too comprehensive, too long and too general. It is felt that they do not give sufficient detail on how to actually undertake HTA in the methodological area(s) within the guideline.

NoMA do, however, report that they will always have a look at new or updated EUnetHTA tools and guidelines. If they fit into their national guidelines, they will then consider using or implementing them.

Examples of use of EUnetHTA guidelines by NoMA have included:

- Review of evidence submission template to inform the development of their own submission template.
- The guideline on direct and indirect comparisons has been used as inspiration inform the development of their own national guideline in this area.
- National guidelines for information retrieval for systematic reviews has been checked against the EUnetHTA guideline on information retrieval for systematic reviews and HTAs on clinical effectiveness to be sure that NoMA doesn't demand more or less than the rest of Europe (and to be sure that NoMA are consistent with the rest of Europe on information retrieval for systematic reviews).

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

NoMA did not identify that any of the EUnetHTA methodology guidelines specifically limit or support their ability to use EUnetHTA assessments. Key factors identified as limiting use of EUnetHTA assessments is the timing and availability of EUnetHTA joint REAs. Only three pharma products have been assessed in a joint REA so far. NOMA has now developed a process for adaptation/ adoption of REAs to national HTA reports and processes and they expect that coming REAs will be re-used.

Priority areas for improvement in EUnetHTA guidelines and methods development

NoMA propose that the methodology guidelines should be more specific on how to address the topics. From the perspective of NoMA they are too general and do not address in depth specific methods that are necessary to perform the assessment of the submitted documentation.

Guidelines on indirect treatment comparisons especially matching adjusted indirect comparisons (MAIC) would be helpful. It is increasingly common for companies to submit a MAIC to NOMA.

RIZIV INAMI - Belgium

Introduction

Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering / Institut National d'Assurance Maladie Invalidite (RIZIV-INAMI) is the Belgian Healthcare Insurance agency. It produces health technology assessments used to inform decisions about the reimbursement status of pharmaceutical and non-pharmaceutical medical technologies (including medical devices and also any other technologies that may be procured from a hospital or public pharmacy) in Belgium.

Working practices

The role of RIZIV-INAMI is to coordinate and support (technically and legislatively) the decision-making procedures for the reimbursement of health technologies. This includes organising meetings and supporting the Committee that is charged with providing advice about the reimbursement of health technologies to the decision-maker (for pharmaceuticals the Committee who makes the advice is known as the Commission for the Reimbursement of Medicines). For pharmaceutical technologies, the decision maker who receives the advice from the Commission is the Minister of Social Affairs.

In Belgium the reimbursement process is initiated with a company submission. For new products and products with a claim of added value the submission can occur once a product receives CHMP positive opinion. Following submission RIZIV-INAMI staff prepare an assessment using evidence from the application and other sources. The assessment forms that basis of a proposal for reimbursement that is developed by the Commission for the Reimbursement of Medicines. For new products where there is a claim for added value the draft assessment will be sent to an external expert (for a procedure like peer review) as well as going to the Commission.

The Ministerial decision is based on 5 criteria: added therapeutic value, price, budget impact, medical and social needs (place in the treatment pathway) and cost effectiveness, therefore assessments include clinical effectiveness and economic information.

HTA and pricing procedures occur in parallel. The procedure is tied to the 180 days in the Transparency Directive. RIZIV have 90 days to produce a final assessment report, but before this provide a draft report to the company for their response. Therefore, a draft report has to be prepared within 60 days. There is then a subsequent 60 days for the Commission to develop the final reimbursement proposal. Finally, the Minister will take a decision on reimbursement within 30 days (taking into account additional advice from the administration of Finance and the Minister responsible for the Budget).

Involvement in developing EUnetHTA tools and methodology guidelines

Under JA1 RIZIV-INAMI was a reviewer on the EUnetHTA guideline on: *Endpoints used for REA: Safety.*

Use of EUnetHTA tools and methodology guidelines

RIZIV-INAMI has used the following EUnetHTA methodological guidelines:

- Endpoints used for Relative Effectiveness Assessment: Clinical endpoints – Informal use
- Endpoints used for Relative Effectiveness Assessment: Health-related quality of life and utility measures – Informal use
- Endpoints used for Relative Effectiveness Assessment: Safety – Informal use
- Endpoints used for Relative Effectiveness Assessment: Composite endpoints – Informal use
- Endpoints used for Relative Effectiveness Assessment: Surrogate endpoints – Informal use
- Comparators and comparisons: Direct and indirect comparisons – Informal use
- Comparators and comparisons: Criteria for the choice of the most appropriate comparator(s) – Informal use
- Levels of evidence: Applicability of evidence for the context of a relative effectiveness assessment – Informal use.

The guidelines are used informally as required by the agency when undertaking HTA, dependent on the topic, the assessment and the specific decision problem(s). They are not formally incorporated into any procedures.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

All of the EUnetHTA methodological guidelines used by RIZIV-INAMI were identified as significantly supporting use of EUnetHTA assessments at a national level. EUnetHTA assessments are viewed as being undertaken to a high quality with use of established methods – this promotes use nationally.

RIZIV-INAMI have used nationally the EUnetHTA assessments on Midostaurin and MammaPrint. The use of EUnetHTA methodology in the assessments, was identified as making it easier for the agency to use the assessment in a national report.

Priority areas for improvement in EUnetHTA guidelines and methods development

Development of EUnetHTA methods guideline on GRADE.

Methods to deal with evidence gaps (e.g. through areas such as real-world evidence).

Review EUnetHTA guidelines to see if they need to be updated, in light of changes to existing methods or the development of new methods.

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.

Working practices

SMC is involved in the assessment, appraisal and decision-making stages of HTA, but does not cover scoping. 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. 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.

The advice from SMC is disseminated to the 14 NHS Scotland 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.

Involvement in developing EUnetHTA tools and methodology guidelines

SMC have been participating in EUnetHTA since JA2. SMC has been a reviewer and observer on a number of EUnetHTA pharmaceutical assessments published under JA2 and JA3.

To date SMC has not been involved in the development of any EUnetHTA tools and methodology guidelines.

Use of EUnetHTA tools and methodology guidelines

SMC report use of one of the EUnetHTA tools, the POP database. SMC regularly input projects into the POP database. However, SMC do not regularly use the POP database to check what projects other agencies are undertaking.

SMC report use of one of the EUnetHTA methodology guidelines, the guideline on *Comparators and comparisons: Direct and indirect comparisons*. SMC used the

guideline to help inform the development of their own national methods guide on direct and indirect treatment comparisons.

SMC has not explicitly decided not to use or discounted the use of any EUnetHTA methodology guidelines. SMC has not had reason to use most of the EUnetHTA methodology guidelines. SMC have established methods that pre-date the publication of the EUnetHTA methods guides. SMC will consider using EUnetHTA methods as and when they think they are needed, for example when developing methods in new areas such as direct and indirect treatment comparisons.

SMC recognise that EUnetHTA methodology guidelines can be very useful for countries with less developed HTA systems and methods.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

SMC did not identify in the online survey or interview that any EUnetHTA methodology guidelines specifically support or limit use or uptake of EUnetHTA assessments.

Because SMC review all new medicines, the principal factor limiting use of EUnetHTA assessments is timing (not methodology). SMC try to publish advice as soon as possible after marketing authorisation, and often the timing of EUnetHTA assessments are too late for national use in Scotland. To date the principal uses of EUnetHTA assessments by SMC has to been to validate company submissions for Midostaurin (PTJA01), Regorafenib (PTJA02), and Alectinib (PTJA03).

Priority areas for improvement in EUnetHTA guidelines and methods development

SMC identified a need to develop methodological guidelines in complex and challenging methodological areas and in new methodological areas.

SMC would welcome EUnetHTA guidance around undertaking appraisal of emerging 'one and done' technologies (e.g. CAR-T therapy, ATMPs) and tissue agnostic therapies.

Guidance in some areas, for example direct and indirect treatment comparisons, is fast moving so guidance needs to regularly be reviewed and updated, with new guidance developed as appropriate and existing guidance updated in a timely manner.

Sector for Quality, Accreditation and Health Technologies - Croatia

Introduction

The HTA department in the Sector for Quality, Accreditation and Health Technologies (formerly AAZ, until December 2018) within the Croatian Ministry of Health produces national HTA for a wide range of health technologies to support decision-making by the Croatian Health Insurance Fund (CHIF), the Ministry of Health and hospital managers.

HTA in Croatia is not currently mandatory. Therefore, decision makers do not have to use HTA or request HTA from the HTA department. The HTA department is requested to provide HTA in situations where the decision makers require further information to inform their decision.

The HTA department produces approximately eight multiple technology assessments per year, including involvement as authors and co-authors on EUnetHTA reports. Reports can include relative effectiveness assessment only or full comprehensive assessment (but without primary full economic analysis).

Working practices

Requests for assessment come from the Ministry of Health, CHIF or hospital managers. The HTA department have a topic proposal form which institutions submitting requests may use to describe the topic and research question that they want addressed.

The HTAs are produced by staff within the HTA department. The reports include information about the condition, the technology, clinical evidence, cost and a summary of published cost effectiveness evidence. For non-pharmaceutical health technologies relevant information about organisational, legal, social and ethical issues will also be added to the report. The type of information added is based on a shorter adapted version of the assessment elements in the EUnetHTA HTA Core Model. Where possible the assessment will make use of existing HTA assessment either created by EUnetHTA or another national agency.

Until December 2018, AAZ included recommendations in their report. These include information about the use of a technology and also how a technology should be used. New ordinance on HTA is expected soon with clear regulation on this issue. Once the HTA department have delivered a report they are not involved in the decision making.

For pharmaceutical assessments the HTA department must deliver their report one month after the request, which is possible only if appropriate recently published (by EUnetHTA or another national agency) report is available for adaptation. For non-

pharmaceutical health technologies timeframes are not defined by law and can be negotiated.

Involvement in developing EUnetHTA tools and methodology guidelines

The HTA department at the Croatian Ministry of Health (formerly AAZ) was involved in the revision of the full HTA Core Model in JA2. They have not been involved in the development of any EUnetHTA methodology guidelines. Several EUnetHTA joint REA assessments have been adapted for national use in Croatia.

Use of EUnetHTA tools and methodology guidelines

The HTA department at the Croatian Ministry of Health reported that they use all of the EUnetHTA tools and methodology guidelines. The HTA Core model was incorporated into and written into the Croatian Methods manual published in 2011. HTA. No consultation or legal changes were required to incorporate the HTA Core Model. National reports do, however, need to be in Croatian so translation was undertaken. An update of the Croatian methods manual is planned in the near future.

EUnetHTA methodology are reported to be used by the HTA department informally as and when required for the specific assessment and topic area. EUnetHTA methodology guidelines are particularly helpful in complex and new methodological areas.

In Croatia there has been limited use of the EUnetHTA guideline on economic evaluation as in Croatia they do not undertake primary economic evaluation because it is not mandatory in Croatia.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

It was identified in the survey undertaken for the case study that all EUnetHTA methodology guidelines support national use of EUnetHTA assessments. None of the EUnetHTA guidelines were identified as limiting use of EUnetHTA assessments. The clarity and transparency that they give in terms of the methods used and the reasons were identified as the principal factors supporting use. National adaptation is felt to be much easier when methods are clear.

Priority areas for improvement in EUnetHTA guidelines and methods development

A need for clear links to updated and new scientific and methodology guidelines was identified, so that they know when new guidelines are available or existing guidelines have been updated.

UCSC Gemelli - Italy

Introduction

The HTA Unit in the Agostino Gemelli University teaching hospital (Fondazione Policlinico Universitario Agostino Gemelli IRCCS) is part of the Universita' Cattolica Del Sacro Cuore (Catholic University of the Sacred Heart, Rome – UCSC). It has been involved in the production of HTA since 2001. It produces HTA for medicinal products and other medical technologies (medical devices, medical equipment and diagnostic tests) to inform decisions about procurement, budgeting, pricing (where possible) and use of medical technologies in clinical practice within the specific context of the University Hospital. As part of the process of budgeting, it works with clinicians not only to support introduction of new technologies but also to identify areas for disinvestment to ensure that additional costs are managed. The HTA unit carries out approximately 50 assessments of medical devices and 30 assessments of pharmaceuticals each year.

Working practices

Proposals for new technologies to be introduced are formally submitted to the HTA Unit by doctors within the hospital. Possible topics for disinvestment are identified by a working group who periodically reviews the hospital formulary and medical devices list. When carrying out an assessment UCSC look for existing assessments before they carry out their own assessment. For pharmaceuticals, they are mostly able to use and adapt existing assessments, but for other medical technologies they more often have to develop their own assessment. The HTA that they produce can include information for all the domains of HTA, but only includes ethical, legal, and social information if needed. Economic information includes cost and budget impact. The reports include a recommendation about whether the technology should be introduced and if it is recommended if restrictions or conditions should be applied. The reports produced by the HTA unit inform a decision maker which is a committee within the University Hospital, reports are disseminated internally.

Involvement in developing EUnetHTA tools and methodology guidelines

UCSC Gemelli was involved in the definition of the HTA Core Model and the Core Model for rapid assessments.

UCSC-Gemelli was a co-author on the EUnetHTA Guideline on methods for health economic evaluation.

UCSC-Gemelli was a co-author at the beginning of the development of the EUnetHTA methodology guideline on direct and indirect treatment comparisons (there was then a change in the composition of the working group).

UCSC-Gemelli has also been involved in the development of hospital based HTA EC projects, which has focussed on methodology for hospital based HTA (ADOPHTA, IMPACT HTA, INTEGRATE HTA).

Use of EUnetHTA tools and methodology guidelines

POP database: UCSC-Gemelli use it to check for technologies that other agencies have already evaluated and also populate the database with their ongoing projects (normally update twice per year). The POP database has provided opportunities for collaboration and resulted in information sharing on assessments for UCSC-Gemelli.

EVIDENT database rarely used and is currently offline.

HTA Core Model: UCSC Gemelli assess all the domains and elements within the HTA Core Model. The HTA Core Model is used both in the scoping and assessment of the technology.

HTA Adaptation Toolkit: UCSC-Gemelli look at how relevant and transferable elements of a EUnetHTA assessment are when undertaking an assessment.

Evidence Submission Template: USCSC-Gemelli use the EUnetHTA template to inform the structuring and development of their own internal submission template.

EUnetHTA methods generally are aligned with the hospital based HTA methods. UCSC-Gemelli do not currently have a formal methods guide. UCSC-Gemelli use the following EUnetHTA methodology guidelines on an informal (as required) basis:

- Process of information retrieval for systematic reviews and HTAs on clinical effectiveness
- Endpoints used for Relative Effectiveness Assessment: Clinical endpoints
- Endpoints used for Relative Effectiveness Assessment: Safety
- Endpoints used for Relative Effectiveness Assessment: Composite endpoints
- Endpoints used for Relative Effectiveness Assessment: Surrogate endpoints
- Comparators & Comparisons: Criteria for the choice of the most appropriate comparator(s).

Use of EUnetHTA methodological guidelines is dependent on the nature of the assessment being undertaken. For example, UCSC-Gemelli have yet to undertake indirect comparisons for rapid assessments, so have not considered the use of this guideline.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

Limited impact on uptake party because UCSC is aligned with EUnetHTA. Also, the recommendations in the guidelines are viewed as being quite 'soft' and not prescriptive. Some of the EUnetHTA guidelines are useful to introduce a topic but they are not really a guideline and do not provide practical guidance or recommendations. Examples of such guidelines are: the guideline on direct and indirect treatment comparisons; the guideline on personalised medicine; and the guideline on information retrieval.

Priority areas for improvement in EUnetHTA guidelines and methods development

- Review and update the EUnetHTA guideline on personalised medicine
- Develop guidance on HTA of complex technologies (e.g. medical devices combined with pharmaceuticals, digital health)
- Develop guidance on real-world evidence (maybe link with WP5 on registries)
- Consider how to integrate HTA with patient perspective
- Consider sources of evidence to cover each HTA domain (included organizational, ethical, legal ones).

UNIBA – Slovakia

Introduction

The Constitution of the Slovak Republic guarantees all its inhabitants universal and free access to a wide package of basic health care covered by the public health insurance system. All residents are insured, and they pay a contribution to the public health insurance fund, which is operated by health insurance companies. In Slovakia, a pluralistic system of health insurance companies is in place and three 3 insurance companies currently operate in the Slovak market.

HTA is still a relatively new concept in Slovakia and the country is in the early stage of its implementation. In 2012, the Working Group for Pharmacoeconomics, Clinical Outcomes and Health Technology Assessment of the Slovak Ministry of Health was established. In Slovakia, a single application is filed for both the pricing and the reimbursement of medicinal products.

Working practices

UNIBA FoF is a producer of HTA with a national remit. UNIBA-FoF mainly undertake assessments of pharmaceuticals. Only single technology assessments are undertaken, as UNIBA-FoF is responsible for the assessment of new drugs. It is mandatory for pharmaceutical companies to submit reimbursement dossier that includes both relative effectiveness and pharmaco-economics dossiers.

UNIBA-FoF make HTA recommendations to the Union Health Insurance Fund, which is a member of the national Reimbursement Committee. Based on the recommendations from the Reimbursement Committee, the Ministry of Health issues final decisions. The final reimbursement decisions about new medicinal products are taken by the Slovak Ministry of Health within 180 days from submission of the reimbursement dossiers by manufacturers based on the Transparency Directive (Council Directive 89/105/EEC).

Involvement in developing EUnetHTA tools and methodology guidelines

UNIBA-FoF has been involved in EUnetHTA since JA2. UNIBA FoF participated in the development of the EUnetHTA guideline on methods for economic evaluation published under JA2. UNIBA-FoF has also been involved in the development of a number of EUnetHTA REA assessments, both as co-author and dedicated reviewers.

Use of EUnetHTA tools and methodology guidelines

UNIBA-FoF reported that they use all of the EUnetHTA tools and 12 of the 15 methodology guidelines. The guidelines that they have not used are the guidelines on methods for economic evaluation, therapeutic medical devices and personalised medicine and co-dependent technologies. The economic evaluation guideline has not been used as they already have existing pharmaco-economic guidelines in Slovakia. The guidelines on therapeutic medical devices and personalised medicine and co-dependent technologies have not been used as UNIBA have yet to assess topics in these areas.

The EUnetHTA methods guidelines are used as recommended approaches and are referenced in national guideline and procedures, they have not been formally incorporated into national legislation.

UNIBA are using the Evidence submission template and this has been translated in Slovakian. UNIBA-FoF require companies to use the EUnetHTA submission template and use EUnetHTA guidelines to evaluate the data submitted.

UNIBA-FOF report that the adoption of EUnetHTA tools and guidelines into national methods has supported UNIBA-FoF to improve the quality of HTA procedures, as HTA is still a new and developing concept in Slovakia.

Impact of EUnetHTA methodology guidelines on the use of EUnetHTA assessments

UNIBA-FoF identified that all of the EUnetHTA guidelines that they use *significantly support* their use of EUnetHTA assessments. UNIBA-FoF reported that they felt EUnetHTA guidelines improve the quality of assessments, in turn give more confidence to decision-makers when using the assessments. UNIBA-FoF did not identify any of the EUnetHTA methodology guidelines as limiting their ability to use EUnetHTA assessments.

Priority areas for improvement in EUnetHTA guidelines and methods development

No priority areas for methodological development were identified. UNIBA-FoF are implementing EUnetHTA tools and guidelines in a developing HTA system, so the agency is currently focussed on adoption of existing methods rather than the development of new methods.