The Pharmaceutical Managers' Institute, 27th September 2018

NCPE Insights 2018

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Deputy Head, National Centre for Pharmacoeconomics

National Centre for Pharmacoeconomics

Outline

- Update on NCPE in 2018
- Insights on Rapid Review and HTA process and feedback from NCPE
- Future developments

Outline

- Update on NCPE in 2018
  - **Organisational structure**
  - Timelines
  - Orphan drugs
  - Patient involvement

National Centre for Pharmacoeconomics in Ireland

The NCPE evaluates the clinical and cost-effectiveness of medicines for the Health Service Executive

Mission Statement

Est. 1998:
*to advance the discipline of pharmacoeconomics in Ireland through **practice**, **research** and **education**.*

2018:
...to facilitate healthcare decisions on the reimbursement of technologies, by applying clinical and scientific evidence in a systematic framework, in order to maximise population wellness.

NCPE Organisational Structure

- Period of expansion at NCPE
- Additional Health Technology Assessors
- Specialist roles for orphan drug assessments
- Specialist skills in assessment of cancer drugs
- New roles within team:
  - Statisticians
  - Health Technology Assessment Information Specialists
  - Stakeholder Engagement Lead for Orphan Drugs
  - Senior Health Technology Assessor for Orphan Drugs

The NCPE Evaluation Team: Pre 2018

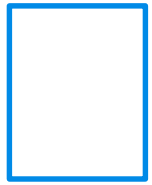
- Medical
- Clinical pharmacy
- Health economics
- Epidemiology/pharmacoepi.
- Statistics







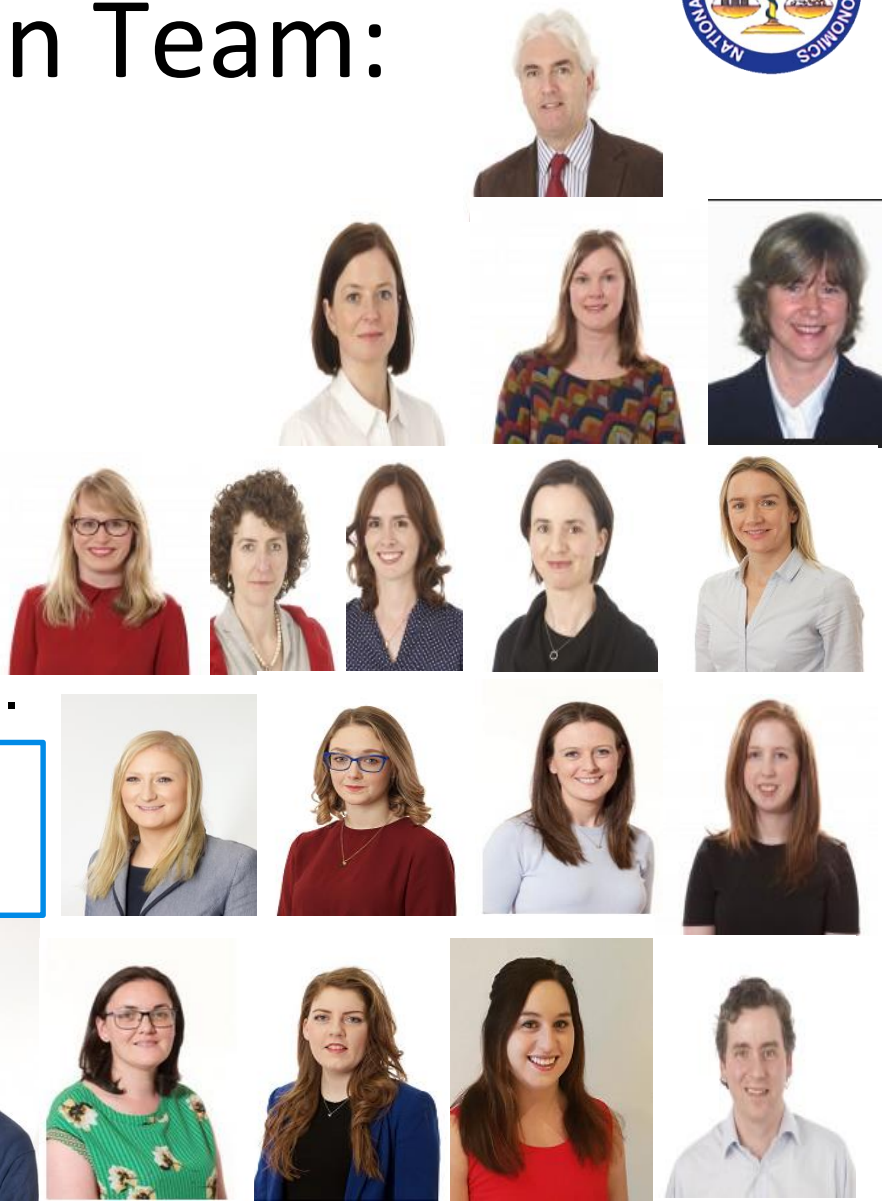






The NCPE Evaluation Team: 2018

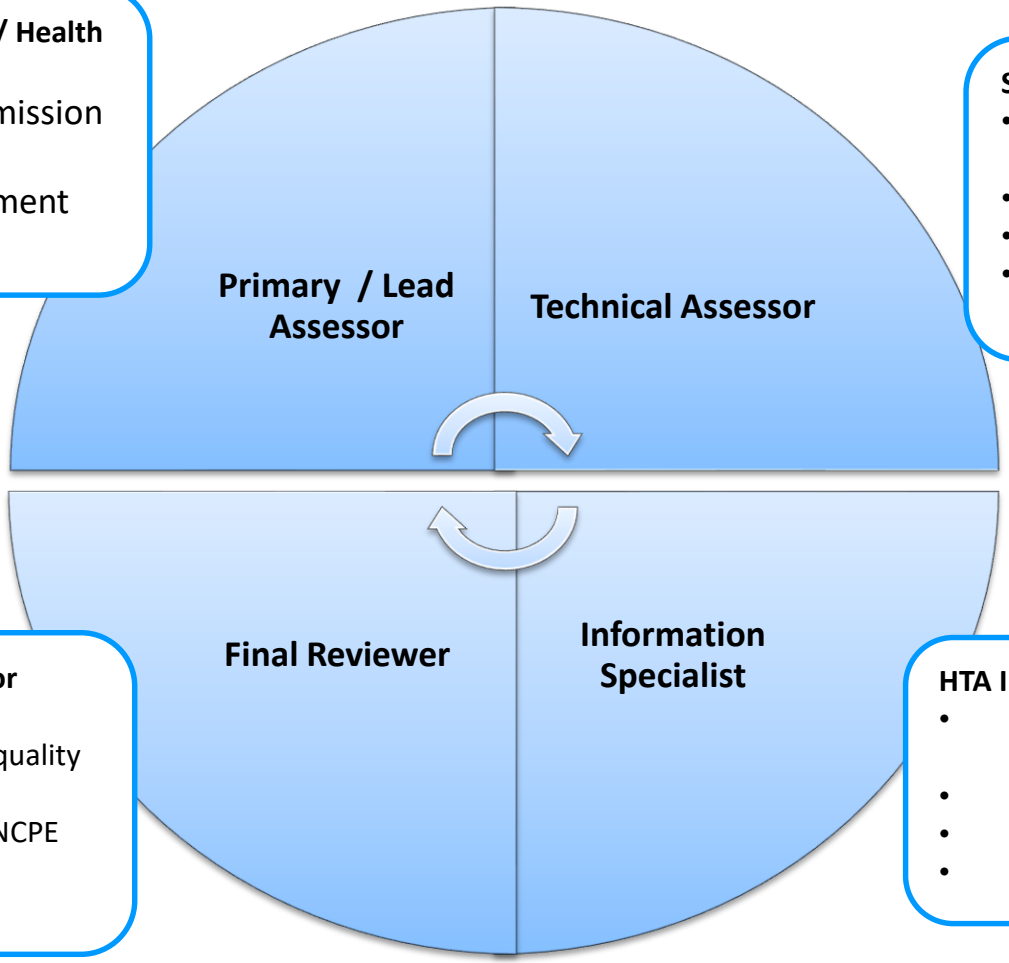
- Medical
- Clinical pharmacy
- Health economics
- Epidemiology/pharmacoepi.
- Statistics



NCPE Evaluation Team

Senior Health Assessor / Health Technology Assessor

- Appraisal of submission
- Report writing
- Clinician Engagement



Statistician / Health Economist

- Appraisal of evidence synthesis / NMA
- Appraisal of model structure
- Appraisal of economic model
- Report writing

Deputy Head / Senior Assessor

- Consistency and quality check
- Final approval of NCPE report and public summary

HTA Information Specialist

- Validation of epidemiology / disease description
- Appraisal of budget impact
- Validate SLR, conduct SLR
- Report writing

Staff Development

Funded PhD program to attract and train staff

- Ensures staff trained in appropriate HTA methodologies
- Promotes culture of research and continued learning

Research component

- Option to pursue relevant research interests and maintain academic positions

Education component

- Encourage continuing professional development of staff

Resource Constraints

An ongoing issue!

- Rapid Review process is a pragmatic approach to managing workload
- Meeting timelines is a challenge
- Staff work on multiple HTAs simultaneously

Outline

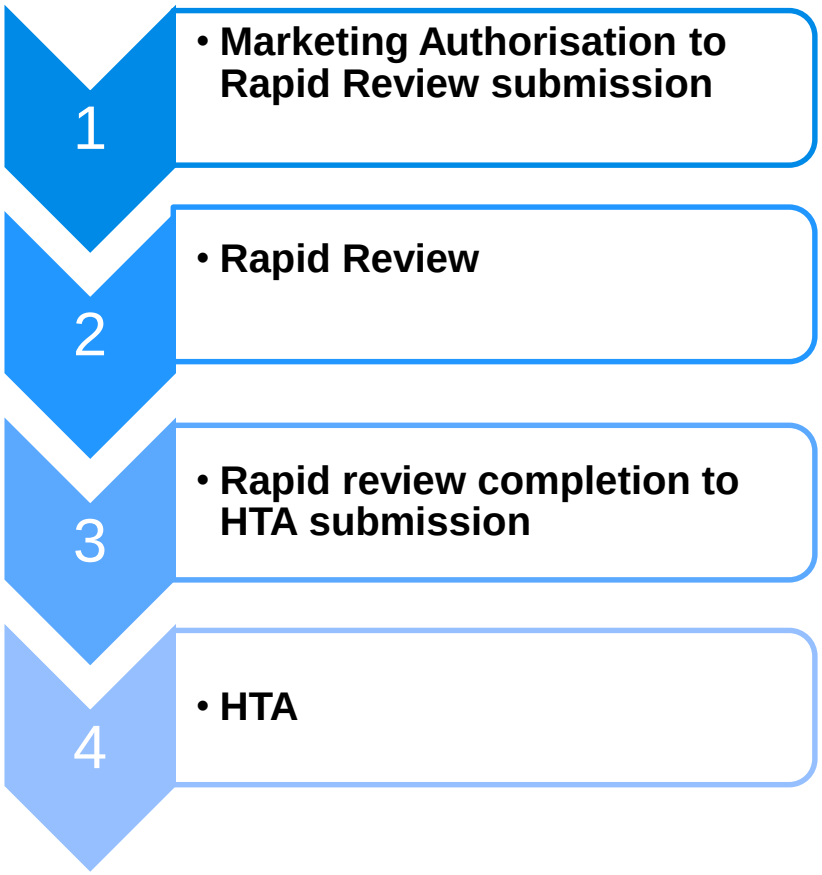
- Update on NCPE in 2018
  - Organisational structure
  - **Timelines**
  - Orphan drugs
  - Patient involvement

Timeline Analysis 2012-2017

- Time from MA to reimbursement is not attributed to a single stage in the process.
- Objective: to investigate timelines for rapid review and HTA submissions from 2012-2017.
- Focus on time from MA to completion of HTA.
- Investigated whether there was any association between different types of submissions and timelines.

Methodology

- All Rapid Reviews submitted to the NCPE between 1st January 2012 and 31st December 2017
- Variables documented : Reimbursement Scheme, orphan/cancer
- Timeline was divided into four stages.
- Analysis conducted using SPSS.



Conclusion

- Rapid Review
  - Results are in line with the 4- week timeframe.
- HTA
  - Number of days substantially longer than 90-day timeframe. When company days are excluded, closer to proposed timeframe.
- There was insufficient evidence to conclude that there was difference in timelines between types of submission
- There are many factors which influence the timeline from MA to reimbursement

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  - Timelines
  - **Orphan drugs**
  - Patient involvement

Update on Orphan Drugs

- Two new staff appointed (Jan 2018):
  - Senior Health Technology Assessor Orphan Drugs
    - Expertise in assessment of orphan drugs
    - Research
  - Stakeholder Engagement Lead Pharmacist for Rare Diseases
    - Patient engagement & clinician engagement activities as part of:
      - HTA process
      - Rare Disease Technology Review Committee (RDTRC)

Planned Projects

- Defining an ultra-orphan product i.e. what drugs will be assessed by the RDTRC
- Examining the impact of broadening the HTA appraisal criteria
- Analysis of decision criteria on reimbursements made to date

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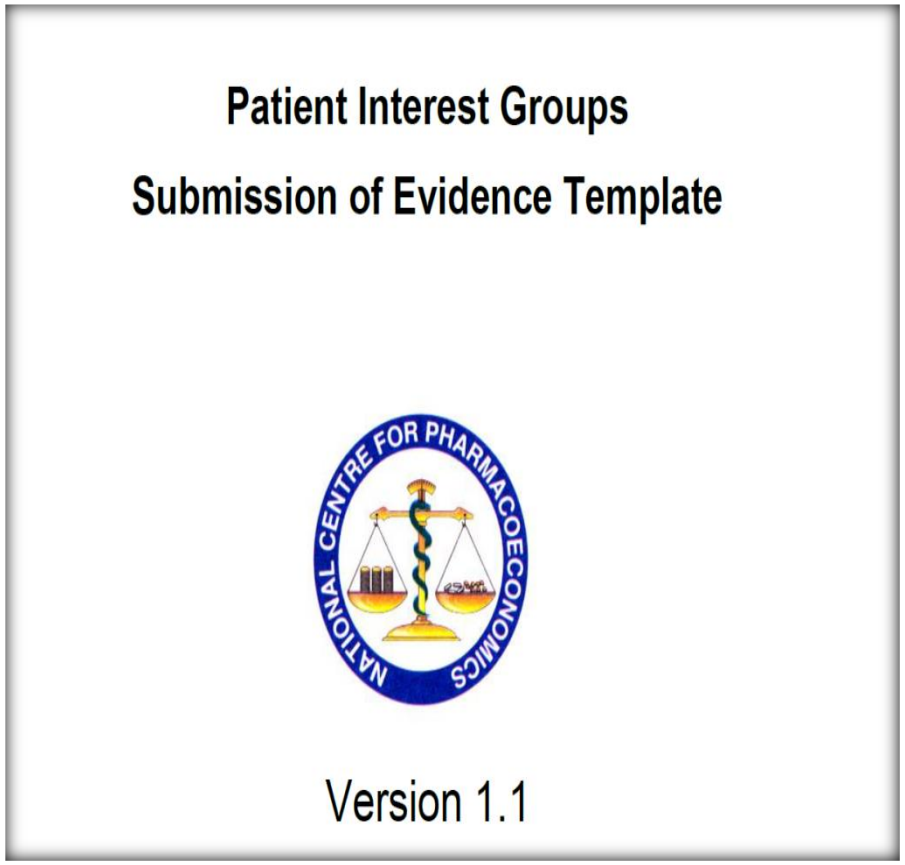
NCPE Engagement with Patient Organisations

Prior to 2014/2015, patient engagement happened, but in an ad hoc and informal manner

- NCPE relationship with IPPOSI
- Meetings with patient groups on request
- Published summaries of HTA on website

Patient Submission Template

- Launched as a pilot March 2016
- 16 submissions by June 2018



Recent Developments

2015/2016
Develop and Launch Patient Submission Template

2017/2018
EUPATI training module in HTA with IPPOSI

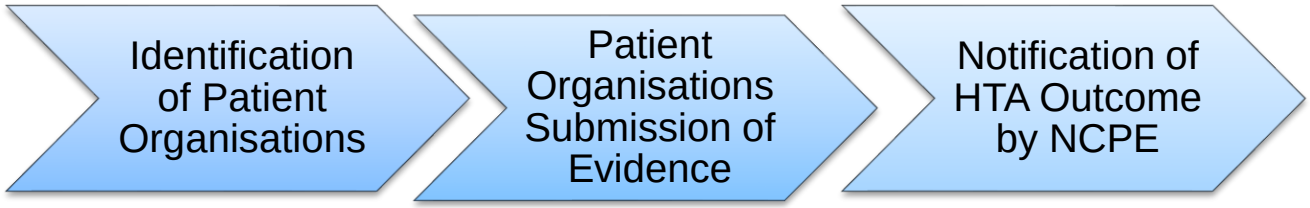
2017/2018
Review of Patient Submission Process

2018
Patient Engagement within Rare Diseases

Updated Patient Submission Process

- Refined patient submission template
- New guidelines on completing template
- New patient database registration form and patient organisations database
- Dedicated point of contact in NCPE
    - For queries on submission process or assistance with template submission

Process Overview: 3 Key Steps



Identification of Patient Organisations

- NCPE will maintain a database of Patient Organisations (POs) to inform them when a relevant HTA has been commissioned
- If no appropriate PO is registered, NCPE will work with IPPOSI and MRCG to identify a suitable organisation
- Will also advertise for patient submissions through website & social media (Twitter).

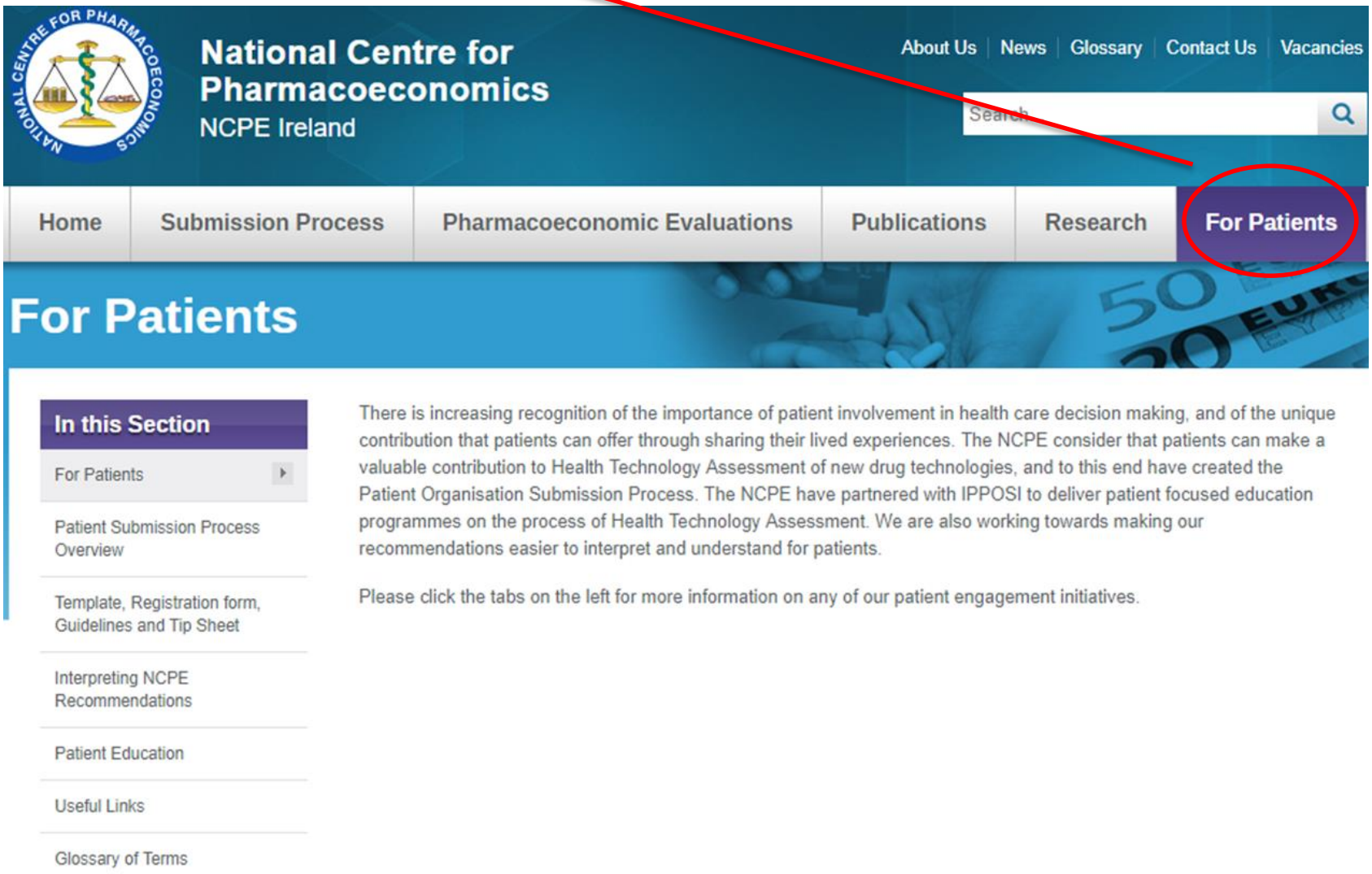
Submission of Evidence

- Detailed guidelines available on submission process, including a step-by-step guide to completing the paitent submission
- The patient submission is included in the HTA final report to the HSE (section 9 and Appendix 1)
- POs must complete and return the template to NCPE within 90 days of the HTA commencing, as recorded on the NCPE website

Notification of HTA outcome by NCPE

- The NCPE will notify the submitting POs of the HTA outcome 48 hours prior to the publication of the summary report on the NCPE website

NCPE Website Update: "For Patients"



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- **Insights on Rapid Review and HTA process and feedback from NCPE**
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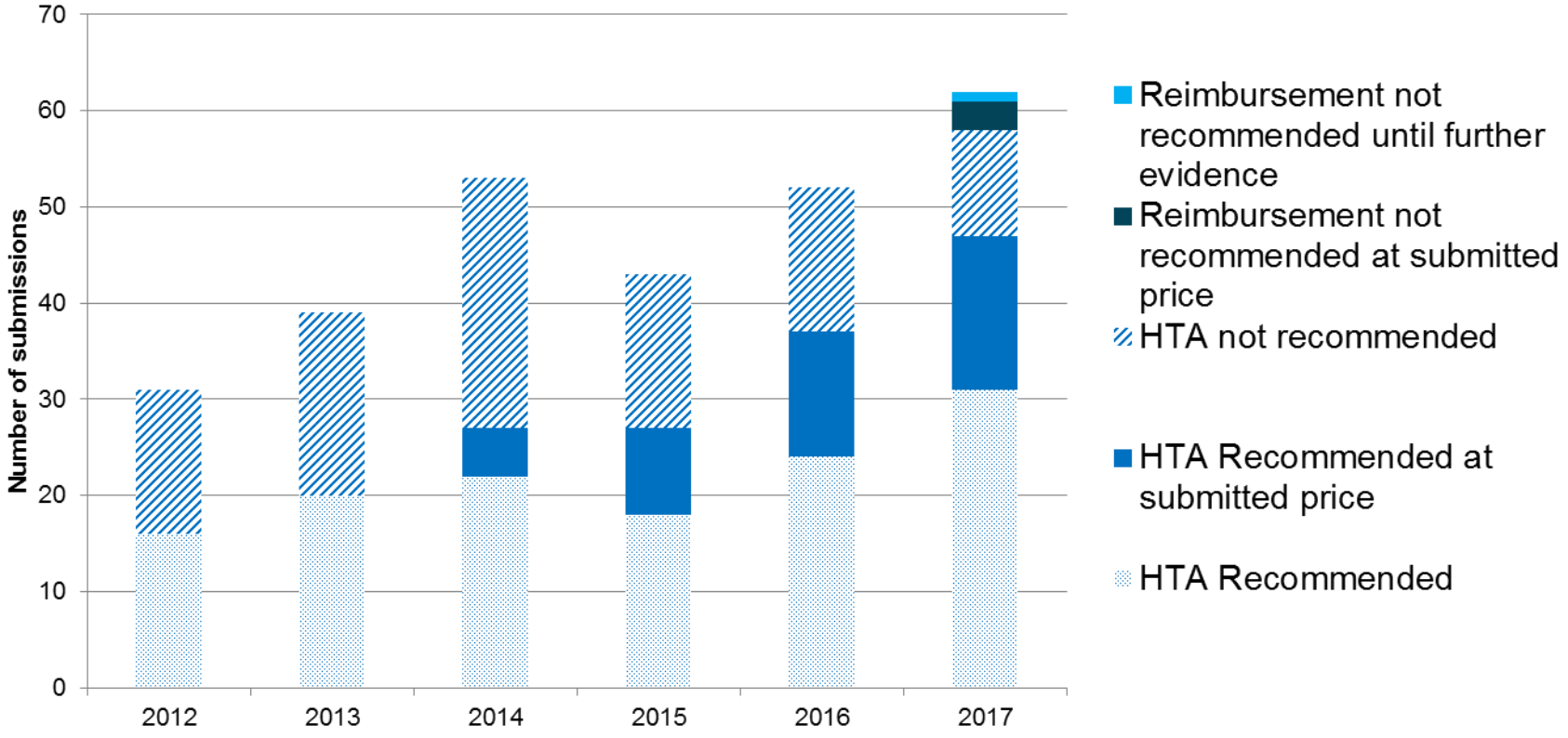
Rapid Reviews and HTAs

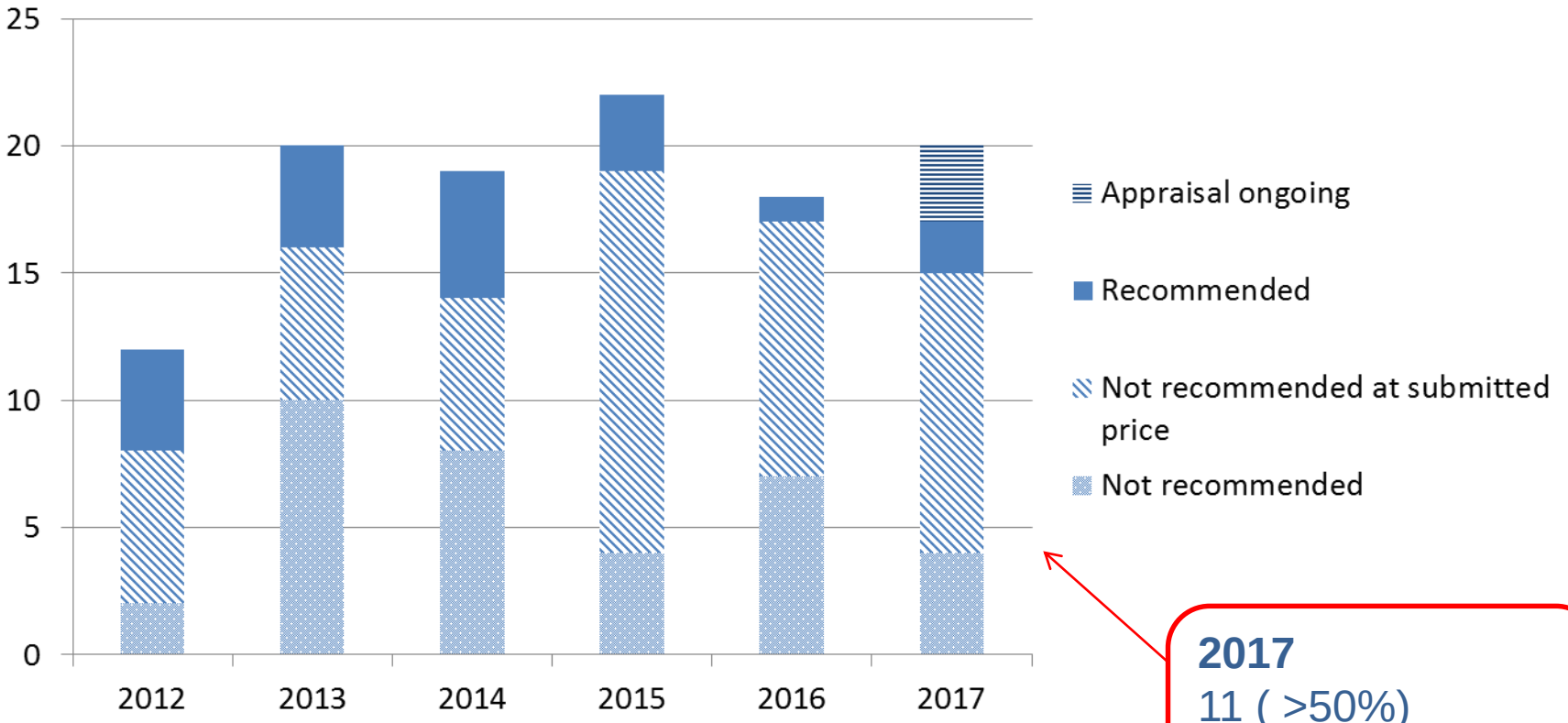
- Increase in volume and complexity continues!
- April 2018: Changes to terminology in NCPE recommendations
- Sept 2018: Update to Guidelines for Inclusion of Drug Costs in Economic Evaluation

Rapid Review Submissions 2012-2017



(n=281)

Full HTA Submissions 2012-2017



2017
11 (>50%) submissions were for orphan drugs

(n=113)

RR and HTA submissions 2018

- 32 rapid reviews
- 17 HTAs submitted / 17 HTAs awaiting submission
- High volume of submissions for cancer indications
- Advanced Therapy Medicinal Products (ATMPs):
  - NCPE Rapid Reviews:

    Tisagenlecleucel (Kymriah®) for DLBCL and ALL

    Axicabtagene ciloleucel (Yescarta®) for DLBCL
  - NCPE Full HTA:

    Darvadstrocel (Alofisel®) for rectal fistula

Feedback on Rapid Reviews

- To ensure timely assessments – balance complexity with the intended rapid nature of these assessments
- Possible to include details of a PAS at this stage
- The RR is the only formal evidence based assessment for those drugs that don't require a full HTA

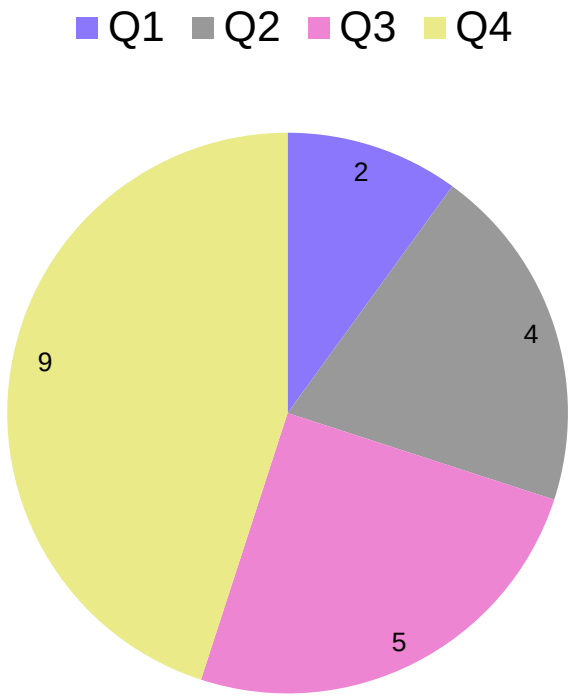
Feedback on HTAs

- Evaluation Team
  - Quality check reports before submitting
  - Ensure workable version of model submitted
- Statisticians
  - Collaboration with other HTA agencies (SMC).
  - Common methodological issues identified
  - Shared concerns in relation to reporting of methods of indirect treatment comparison
  - A number of areas where further information is routinely requested from companies

HTAs: Challenges

- Timelines
- Early regulatory approval; limited evidence
- Statistical methods of indirect comparison in the absence of RCT evidence
- Affordability: For example
  - PCSK9s
  - Immunotherapies
  - ATMPs: gene therapies, cell therapies and tissue engineering products

Timing of Full HTA Submissions 2017



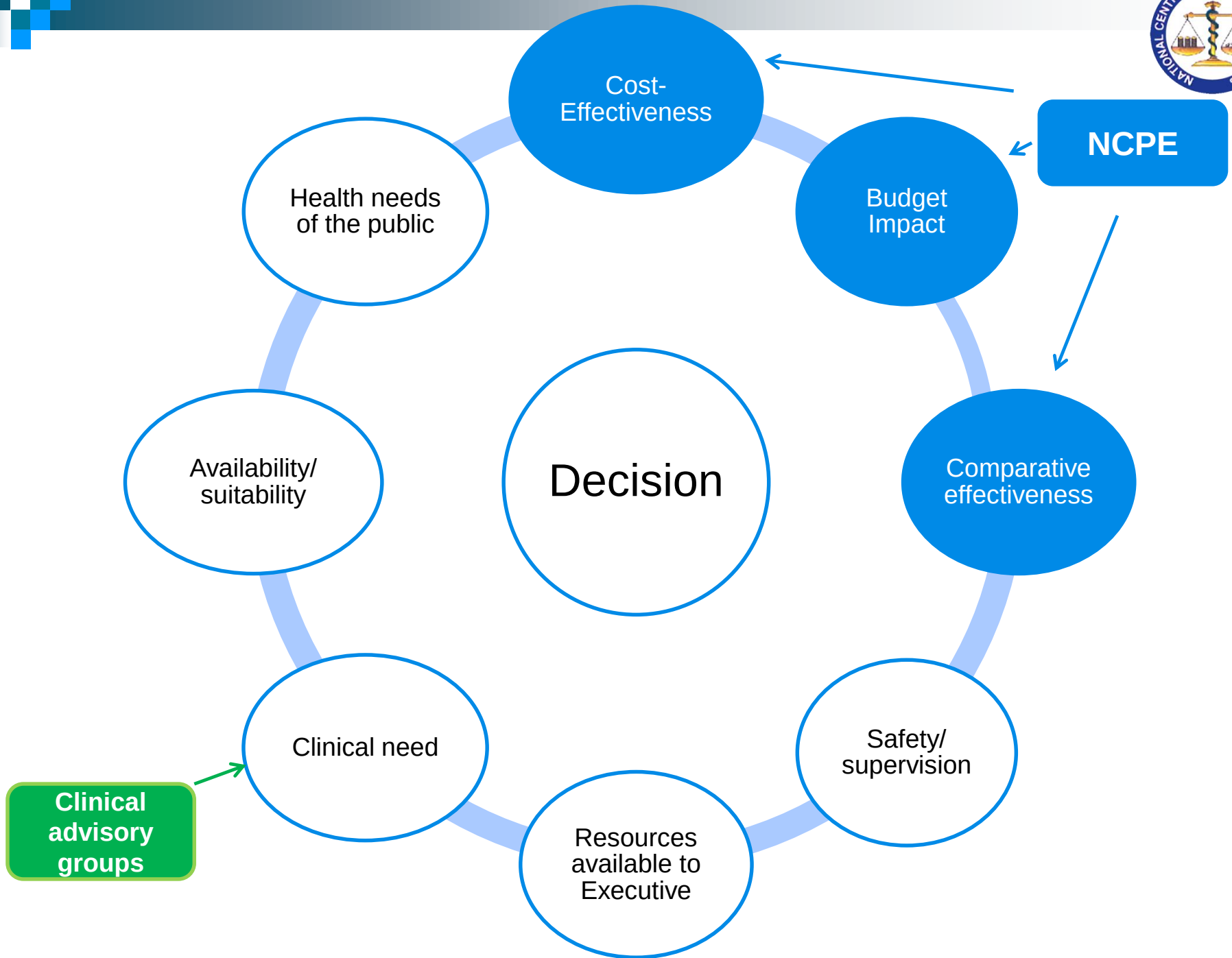
45% of HTAs were submitted in Q4 2017

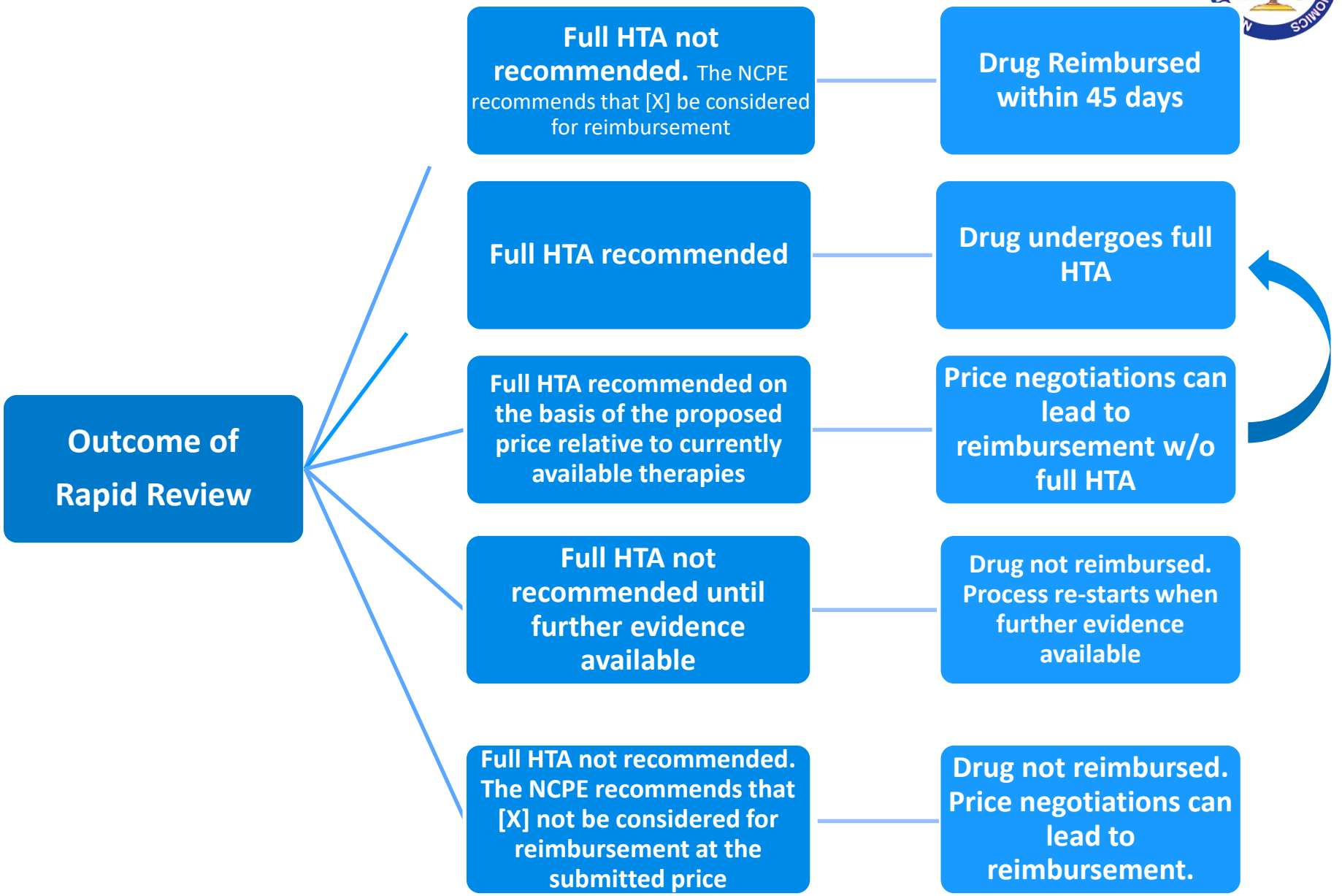
HTA of Advanced Therapy Medicinal Products

- Short “one-off” treatment regimen promising lifelong benefits at a very high cost
- Challenges specific to clinical evidence, value assessment and budget impact
- Various published reports outlining possible new approaches to payment including
  - Long-term amortisation of initial costs
  - Risk sharing / outcomes based payments

New Terminology for NCPE Appraisals

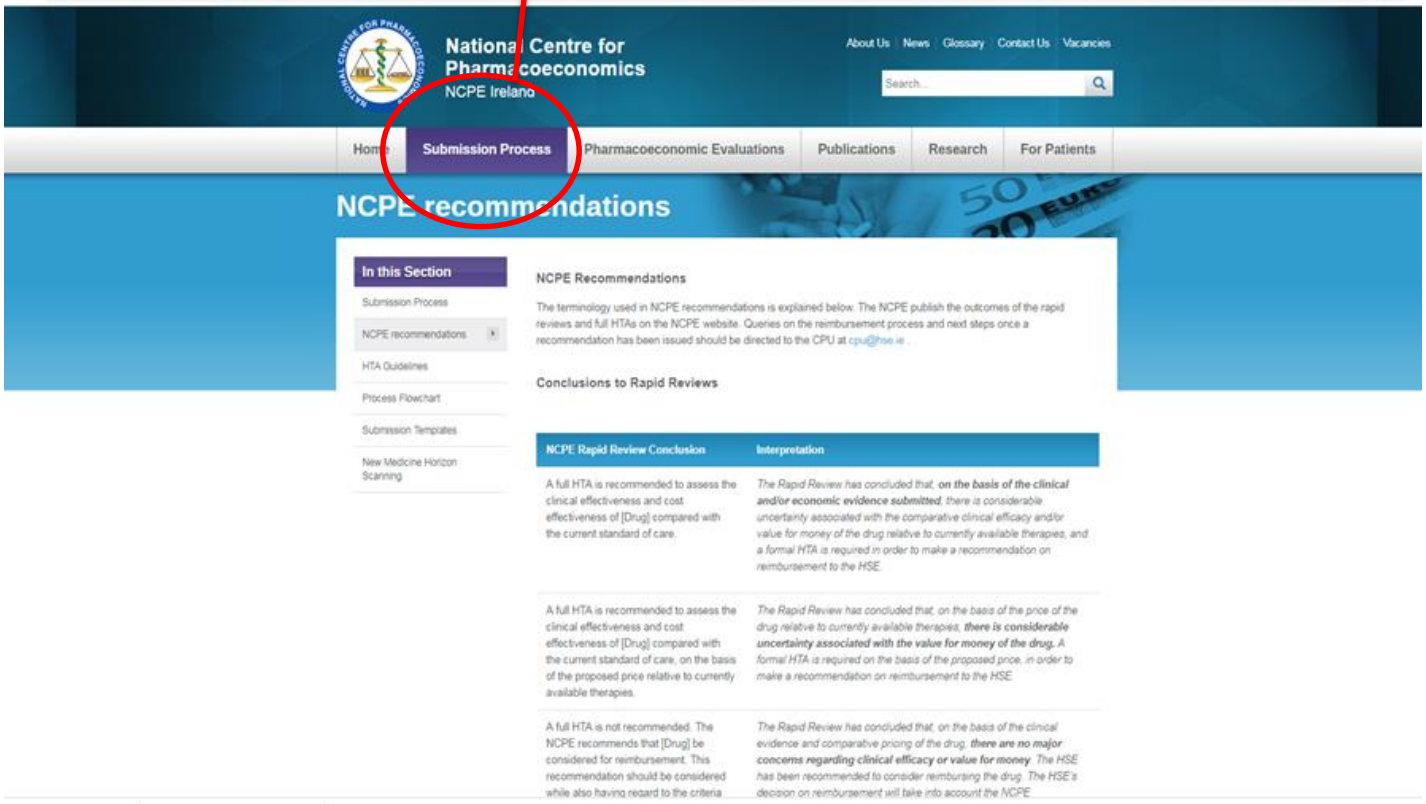
- Recently changed the phrasing of our recommendations in order to better reflect the nuances of the decision making process.
- Stress the vital role of the Health Act in determining reimbursement decisions
- HSE Drugs Committee consider our **recommendations** in addition to the other criteria included in the Health Act when making their decision


Cost-Effectiveness
NCPE
Budget Impact
Health needs of the public
Comparative effectiveness
Availability/ suitability
Decision
Safety/ supervision
Clinical need
Clinical advisory groups
Resources available to Executive


Outcome of Rapid Review
Full HTA not recommended. The NCPE recommends that [X] be considered for reimbursement
Drug Reimbursed within 45 days
Full HTA recommended
Drug undergoes full HTA
Full HTA recommended on the basis of the proposed price relative to currently available therapies
Price negotiations can lead to reimbursement w/o full HTA
Full HTA not recommended until further evidence available
Drug not reimbursed. Process re-starts when further evidence available
Full HTA not recommended. The NCPE recommends that [X] not be considered for reimbursement at the submitted price
Drug not reimbursed. Price negotiations can lead to reimbursement.

NCPE HTA recommendation	Interpretation
The NCPE recommends that [Drug] be considered for reimbursement. This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.	The NCPE assessment has concluded that the drug represents a clinically effective, value-for-money treatment option, relative to currently available therapies. The HSE has been recommended to consider reimbursing the drug. The HSE's decision on reimbursement will take into account the NCPE recommendation, and the additional criteria listed Schedule 3, Part 3 of the Health (Pricing and Supply of Medical Goods) Act 2013.
The NCPE recommends that [Drug] be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments. This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.	The NCPE assessment has concluded that there is robust evidence for clinical benefit of the drug, and are satisfied that the economic model presented by the company is adequate for decision making. Plausible estimates of the cost-effectiveness of the drug indicate that the incremental cost-effectiveness ratio (ICER) exceeds the current willingness to pay (WTP) thresholds of €20,000 and €45,000/QALY.
The NCPE recommends that [Drug] not be considered for reimbursement unless cost effectiveness can be improved relative to existing treatments. This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.	The NCPE assessment has concluded that either (i) There is robust evidence for clinical benefit of the drug, and the economic model presented by the company is adequate for decision making. Plausible estimates of the cost-effectiveness of the drug indicate that the incremental cost-effectiveness ratio (ICER) far exceeds the current willingness to pay (WTP) thresholds of €20,000 and€45,000/QALY. (ii) There is some evidence of comparable clinical benefit but not additional benefit, and the economic model presented by the company is adequate for decision making. Plausible estimates of the cost-effectiveness of the drug indicate that the incremental cost-effectiveness ratio (ICER) exceeds the current willingness to pay (WTP) thresholds of €20,000 and €45,000/QALY.
The NCPE recommends that [Drug] not be considered for reimbursement. This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.	The NCPE assessment has concluded that relative clinical benefit has not been demonstrated in the submission provided, or the economic evaluation presented is not sufficiently robust to estimate a plausible ICER.

NCPE Website Update: "NCPE Recommendations"



Outline

- Update on NCPE in 2018
- Insights on Rapid Review and HTA process and how to work better with NCPE
- **Future developments**

Guideline Development

- Evidence synthesis / NMA
- Survival analysis

Further Development of stakeholder engagement

- Plain language summaries
- Website development
- Education and training

Into 2018 & 2019

Training / Team Building

Further Development of Submission Templates:

Budget impact template / drug cost calculator - PILOT

EUnetHTA

- NCPE are full partners in EUnetHTA (JA3)
  - Actively participate in all main Work Packages
    - Production of Joint Relative Effectiveness Assessments
    - Early scientific advice to manufacturers
    - Guidelines development and Quality Assurance
    - Implementation
  - March 2018: Oireachtais Committee meeting on the proposed EU legislation for mandatory joint clinical effectiveness assessment
    - Ongoing feedback to DOH in relation to the proposed legislation

BeneLuxA

- June 2018: Ireland formally joined BeNeLuxA initiative
- Four types of HTA collaboration being explored
  - Reuse of HTA reports
  - Joint writing of HTA reports
  - Mutual recognition of HTA reports
  - External referee

Name pharmaceutical	active substance (EMA)	therapeutic area (EMA)	year	Type of HTA-collaboration
LOJUXTA	lomitapide	hyper-cholesterolemia	2015	Re-use of Dutch work by Belgium
ORKAMBI	lumacaftor / ivacaftor	cystic fibrosis	2016 first submission	Joint writing by Belgium & The Netherlands The Dutch Zorginstituut also acted as external referee for RIZIV-INAMI Final report was used by Luxembourg
PRALUENT	alirocumab	dyslipidemias	2016	Dutch Zorginstituut acted as external referee for Belgium RIZIV-INAMI
ORKAMBI	lumacaftor / ivacaftor	cystic fibrosis	2017 second submission	Joint writing by Belgium & The Netherlands The Dutch Zorginstituut also acted as external referee for RIZIV-INAMI Final report was sent to Luxembourg and Austria
VYNDAQEL	tafamidis	amyloidosis	2017	The Dutch Zorginstituut acted as external referee for RIZIV-INAMI Final report was used by Luxembourg

The Table mentions the situation in October 2017.
Abbreviations: RIZIV-INAMI Rijksinstituut voor Ziekte- en Invaliditeitsverzekering Institut National Assurance Maladie-Invalidité(Belgian HTA activities on submitted pharmaceutical files for reimbursement); EMA European Medicines Agency

Source: http://www.beneluxa.org/hta

Conclusion

- Increase in volume and complexity of HTAs continues
- NCPE team is adapting to meet these challenges
- Increased level of patient and clinician engagement
- Innovations such as gene therapies present additional challenges
- Increasing international collaboration on HTA

NCPE Annual Course 2019

Date:15th -16th May 2019

Venue: Dublin Castle

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