HTA in the UK: how it works

Process and case studies

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Topics to be covered

- HTA bodies in the UK
- How NICE process works
  - Process overview
  - Recent changes
  - Pricing of medicines
- NICE case studies (illustrating appraisal decisions)
- How UK HTA bodies differ

HTA in the UK
Three different bodies

England
Pop: 55.6 mill

Scotland
Pop: 5.4 mill

Wales
Pop: 3.1 mill

NICE

National Institute for Health and Care Excellence

SMC

Scottish Medicines Consortium

AWMSG

All Wales Medicines Strategy Group

NICE National Institute for Health and Care Excellence

Overview of the NICE process

How does it work?

National Institute for Health and Care Excellence (NICE)

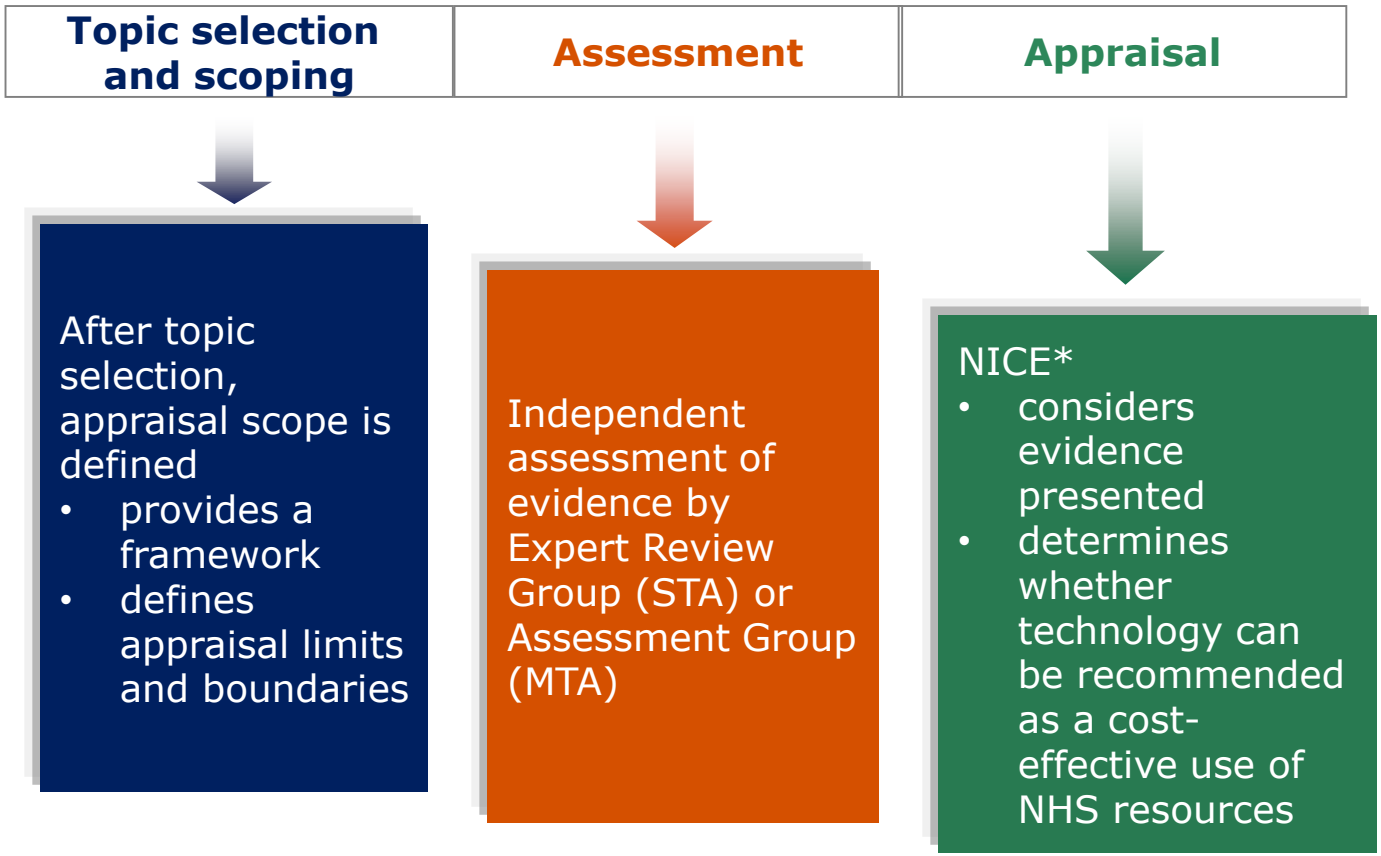
- Established in1999 to reduce “post code lottery” in NHS care
- Covers England and Wales only
- All guidance developed by independent committees of experts including clinicians, patients, carers and health economists
- Multiple work-streams, including:
  - **Technology appraisals** for new medicines, medical devices, diagnostic techniques, surgical procedures, health promotion activities
  - Evidence-based clinical guidelines
  - Public Health Guidance (since 2005)
  - Quality standards for health and social care, eg end of life care for adults
  - Information services

NICE - Several Appraisal Processes

- Single Technology Appraisal (STA)
  - To appraise a single product with a single indication
  - Critical review of manufacturer submission (prepared by the Expert Review Group, ERG, appointed by NICE)
  - Usually takes at least 43 weeks
- Multiple Technology Appraisal (MTA)
  - To appraise multiple products for the same indication
  - Independent assessment (prepared by the Assessment Group appointed by NICE)
  - Slow process takes at least 60 weeks
- Fast Track Appraisal (FTA)
  - To allow quicker access to the most cost-effective new treatments
  - Process reduced to about 32 weeks
- Highly Specialised Technologies (HST)
  - Applies to high cost drugs for very rare conditions
  - Only 1-3 carried out each year (10 published between Jan 2015 and Aug 2019)
- Appraisals are reviewed and updated

The general NICE HTA process

The NICE HTA process is divided into three stages (may be followed by appeal)



*Appraisal committee

NICE – decisions on appraisals

- NICE technology appraisals recommendations made by one of 4 independent Technology Appraisal Committees:
  - Each committee has about 30 members
- Members appointed for 3-year terms and drawn from:
  - National Health Service (NHS)
  - patient and carer organisations
  - academia
  - pharmaceutical and medical devices industries
- Appraisal consultees can make a submission and comment on appraisal
- Commentators cannot make a submission or appeal

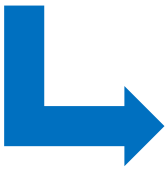
Consultees: company, national patient groups, healthcare professional bodies, Department of Health, clinical commissioning groups, etc; can make a submission
Commentators: comparator companies, research groups, HC Improvement Scotland etc; do not make a submission but can participate in the ACD consultation

https://www.nice.org.uk/get-involved/meetings-in-public/technology-appraisal-committee

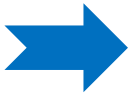
Appraisal Committee decisions
Process up to 1 Apr 17: affordability not considered*

- **Clinical effectiveness**
  - Robust clinical evidence (RCTs, meta-analysis)
  - Clinical practice
  - Safety (AEs)

- **Cost-effectiveness**
  - Economic model
    - Appropriate time horizon, comparators, utility values
    - Most plausible ICER (needs to be ≤£30k)
    - End of life criteria if appropriate (ICER can be up to £50k)



Consideration of the evidence



Decision
(ACD or FAD)

*Although submissions have always included a section on budget impact, this information was not taken in account when making the guidance decision

Other Considerations – End of Life (EOL)

- Criteria
  - Short life expectancy (<24m)
  - 3 month+ gain in overall survival
  - Step change
  - Robust evidence
- Only necessary if ICER is > £20-30k
- In practice, ICERs need to be under £50k/QALY

Other considerations - patient access schemes

- "Can facilitate patient access when NICE's assessment of value, on the current evidence base, is unlikely to support the list price."
- Two types:
  - Simple discounts
  - Complex schemes (eg outcomes-based dose caps, rebates, free stock)
- Department of Health and NICE's PASLU (Patient Access Scheme Liaison Unit) determine suitability for NHS
- Can be submitted
  - As part of initial submission, or
  - After final guidance has been issued, or
  - Under exceptional circumstances, during the appraisal process (but only simple discounts)
- In practice, since August 2011, most schemes have been simple discounts
- Some complex schemes can be considered too burdensome for the NHS to implement

https://www.nice.org.uk/about/what-we-do/patient-access-schemes-liaison-unit

NICE National Institute for Health and Care Excellence

Recent changes to the NICE process

Budget impact test

- Introduced in April 2017
- Applies to TAs and HSTs
- Key aims
  - Take affordability into account in appraisal decisions
  - Mitigate impact of funding technology on NHS
  - Better manage access to new treatments
- Key test
  - Assesses financial impact over first 3 years of use in the NHS
  - Budget impact >£20 million in any of the 1st 3 years results in “commercial discussions” between the company and NHS England

www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/budget-impact-test

NICE fast track appraisal (FTA)

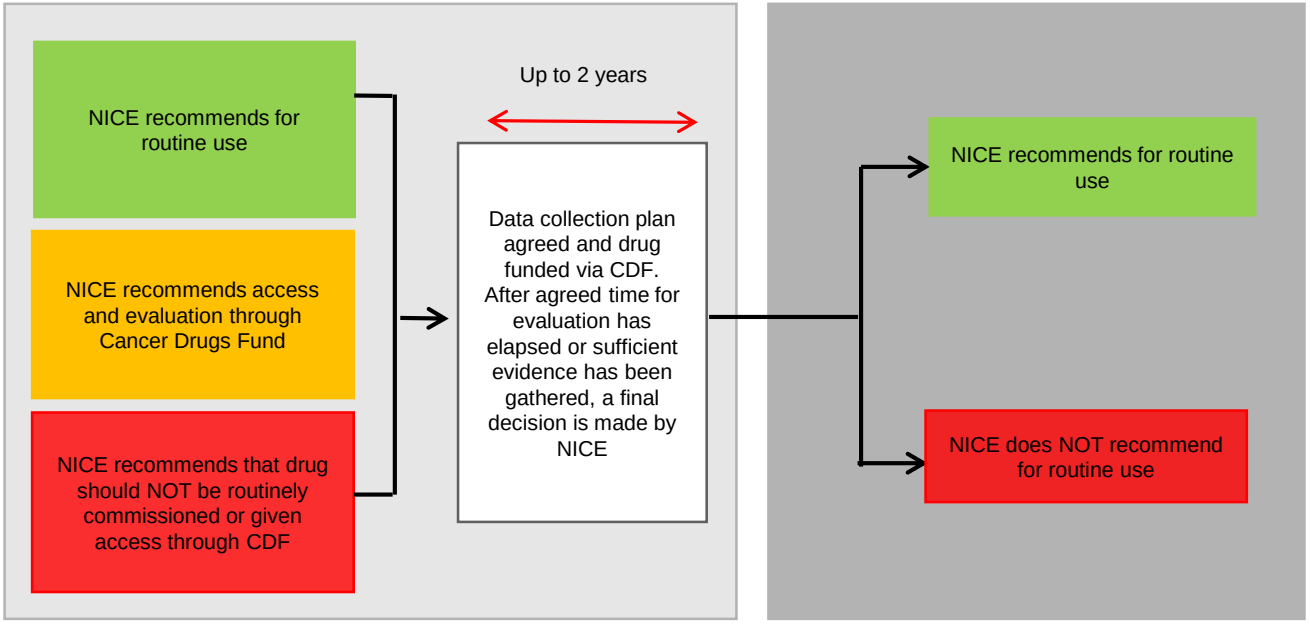
- Introduced in April 2017
- Key aim
  - Quicker access to new, cost-effective treatments
- When it's used
  - Technologies with company base-case ICERs <£10 000/QALY
  - Most plausible ICER <£20 000/QALY

    OR
  - Cost-comparison case shows equal/greater benefit at similar/lower costs for similar technologies
- Appraisal process reduced to 32 weeks from 43 weeks

www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/process

Cancer Drugs process

- Introduced in July 2016
- Submission made to NICE before EMA marketing approval
- NICE can make 3 decisions for cancer drugs: yes, no or provisional yes with data collection
- Key driver: earlier access for promising drugs while additional data are collected
- Key issue: whether sufficient appropriate data can be collected in 2 years



Medicines pricing

How does it work?

How does medicines pricing work?

- Freedom of pricing for list prices of new medicines – just inform DH
- BUT – funding/HTA approval at that price?
- Almost all drugs approved by NICE/SMC/AWMSG rely on confidential discounts (patient access schemes)
- Budget impact test (projected sales >£20 million in any of 1st 3 years) may require additional confidential discounts
- Approval via Cancer Drugs Fund usually includes market access agreement
- The Voluntary Scheme for Branded Medicines Pricing and Access (VPAS, Jan 2019) – guarantees cap in medicine sales growth
- **Actual net prices therefore generally unknown**
- Future pressure from WHO Transparency Resolution (28 May 2019)?

NICE National Institute for Health and Care Excellence

NICE case studies

Examples of appraisal decisions

NICE case study 1

TA590, published July 2019

Drug	Fluocinolone acetonide intravitreal implant
Indication	Treatment of recurrent non-infectious uveitis
List price/£	£5 500 per single implant Simple discount PAS approved
Comparator	Dexamethasone implant
Key issues	• What is the most plausible method of comparison with dexamethasone? • Is retreatment on treatment failure plausible? • Is the modelling of adverse events reliable?
ICERs (£/QALY gained)	Company: £7 183 ERG: £12 325 - £30 153 Scenarios: up to £85 084 (with disutility to 0,1 for AEs)
NICE decision	**Recommended (only if company provides PAS)**

https://www.nice.org.uk/guidance/ta590

NICE case study 2

TA550, published Dec 2018

Drug	Vandetanib
Indication	Medullary thyroid cancer in adults
List price/£	£5 000 per monthly pack Simple discount PAS approved
Comparator	Carbozantinib

Key issues	• Does ‘restricted population’ subgroup reflect
	  • Marketing authorisation?
	  • The way vandetanib will be used in clinical practice?
	• Is the RPSFT crossover adjustment appropriate?
	• Which assumptions are most appropriate for
	  • Choice of parametric curves for extrapolation?
	  • Post-progression vandetanib costs and benefits?
	  • Are EOL criteria met?
	  • What is the most plausible ICER?

NICE case study 2 (cont'd)

TA550, published Dec 2018

Drug	Vandetanib
ICERs (£/QALY gained)	Exact ICER is confidential Most plausible ICER • vs carbozantinib: > £100 000 • vs best supportive care (BSC): >£50 000 Meeting EOL criteria: • Overall survival (OS) benefit > 3 months: yes • Life expectancy < 24 months: no
CDF	Does not meet criteria: Key uncertainty is OS benefit; too few patients to collect sufficient data to address this
NICE decision	**Not recommended:** • Benefit vs BSC uncertain • OS data unreliable • Cost-effectiveness estimates > than acceptable levels • Does not meet EOL or CDF criteria

https://www.nice.org.uk/guidance/ta590

NICE case study 3

TA593, published Aug 2019

Drug	Ribociclib plus fulvestrant
Indication	HR-positive, HER2-negative advanced breast cancer
List price/£	Ribociclib: £2 950 per month Fulvestrant: £522,41 per month Simple discount PAS approved
Comparator	Everolimus plus exemestane
Key issues (original)	• Results based on subgroup analysis of pivotal trial • OS data immature • Extrapolation of progression-free survival uncertain • Post-progression survival
ICERs	Most plausible ICER: significantly above £30 000
NICE decision (original)	**Not recommended** • OS unknown (awaiting final trial results) • Clinical and cost-effectiveness highly uncertain • ICERs much higher than considered acceptable

NICE case study 3 (cont'd)

TA593, published Aug 2019

Drug	Ribociclib plus fulvestrant
Company response	Offered additional discount as a component of managed access agreement (MAA)

Key issues (post-MAA)	• Which cost of electrocardiogram is preferred:
	  • Company (£52,09)?
	  • ERG (£256)?
	• Using the proposed MAA, plausible potential to be cost effective?
	• Can ribociclib + fulvestrant be considered for the CDF?

NICE decision (post-MAA)	**Recommended** for use within the CDF**:** • OS data from pivotal trial available in 2020 • Further data collection could resolve some uncertainties • Plausible potential to be cost-effective • Data collection period should end Dec 2020

https://www.nice.org.uk/guidance/ta593

NICE, SMC and AWMSG

How do they differ?

Main differences between NICE, SMC and AWMSG

	NICE	SMC	AWMSG
Products appraised	Topic selection process: not all products appraised	All new products/ indications/formulations	All new medicines not on NICE work programme
Timelines	Timelines set out but often slip – takes at least 39 wks (STA)	Strict timelines – rapid appraisal (~4m)	21 wks from dossier submission to AWMSG recommendation to ministers
Consultation	Extensive consultation (manufacturers and public can attend meetings)	Some consultation (manufacturers and public can attend meetings	Some consultation (manufacturers and public can attend meetings)
Orphan/ultra-orphans	No allowance for orphan/ultra-orphan designation (except for HST)	Orphan (50)/ultra-orphan (10/100,000) UO: ICER should not be main issue Draft negative: can request PACE (Patient and Clinician Engagement) meeting	Orphan (50)/ultra-orphan (10/100,000) UO: ICER should not be main issue Draft negative: can request CAPIG (Clinician & Patient Involvement Group) meeting
Jurisdiction	STAs apply to Wales; MTAs apply to Scotland and Wales	SMC advice does not apply to England/Wales	AWMSG advice does not apply to England/Scotland
Resubmission	No resubmissions; guidance reviewed according to timelines determined by NICE	Resubmissions are allowed and company can choose when	Resubmissions are allowed and company can choose when