Workshop for additional clinical benefit

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Agenda

- NICE guidelines
- Single arm trial appraisal and key issues
- RCT appraisal and key issues
- Wrap up and discussion

NICE guidance and Committee meeting

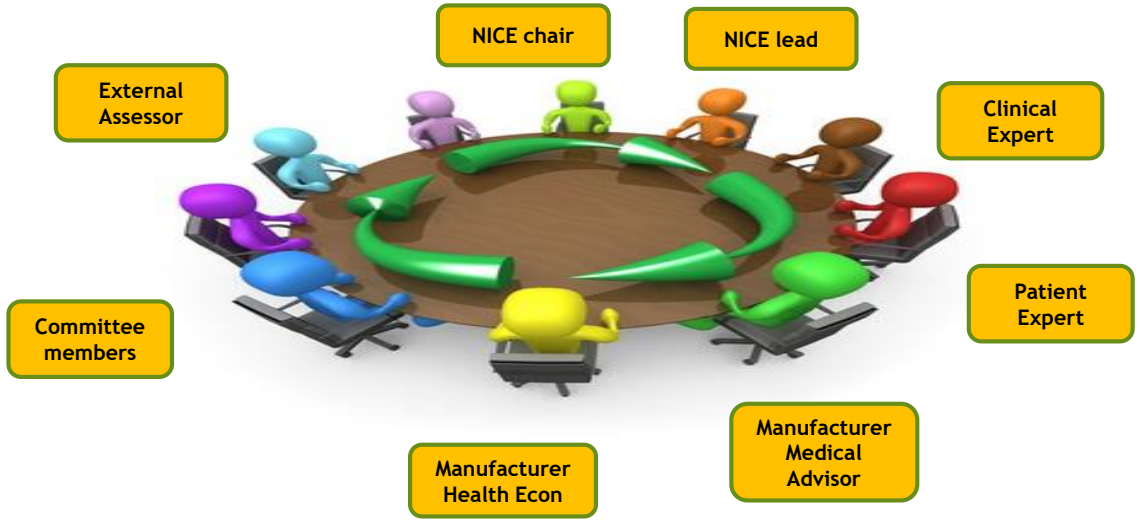
NICE have developed guidelines which is a user guide for submission of evidence

Overall goal https://www.nice.org.uk/process/pmg24/chapter/instructions-for-companies

The guidelines document acts as a user guide to manufacturer and at the same time outlines all the information that NICE want to review

Detailed Information

- Decision problem including scope (population, intervention, comparators, outcomes and study design)
- Approaches in health economic methodologies (i.e. NMAs, survival analysis, cost-effectiveness models etc.)



Abbreviations: NICE: National Institute of Health and Care Excellence; NMA: Network meta analysis;

Single Arm Trial appraisal and Key Issues raised in the evidence based

Case Study from a single arm trial appraisal

Overview of the appraisal

- Drug X is a 1st in class oral therapy treating patients with 3rd line leukaemia; high unmet need therapeutic area
- No active comparators available in the market
- Two phase II single arm trials assessing the clinical efficacy and safety of drug X
- Low number of patients in trials (n=190 pooled) with no UK patients enrolled
- PFS and OS key endpoints but OS 30% maturity
- PROs were collected with PFS utility value calculated to 0,853
- End of life criteria?
  - Does drug X prolongs life for more than 3 months?
  - Is drug X indicated for a small patient population (less than 7000 in all licensed indications)?
  - Is drug X indicated for patients with a life expectancy of less than 24 months?

Abbreviations: PFS Progression Free Survival; OS Overall Survival; UK United Kingdom; PRO Patient Reported Outcomes

Case Study from a single arm trial appraisal

Evidence submitted by the company

- The company submitted evidence from a pooled analysis of the two single arm trials for drug X
- Single arm trial design with no comparator – the company felt that the right comparator was BSC with evidence coming from two sources:
  - The comparator arm of a competitor RCT; and
  - **RWE from a UK registry**
- No formal meta-analysis was plausible but just a naïve comparison
- Survival analysis performed using the pooled trials and extrapolation to lifetime time horizon
- Utility values used PFS=0,853 from the trials and PPS=0,600 from the literature
- End of life criteria? Company claimed they were met
  - Does drug X prolongs life for more than 3 months? YES by 5 months
  - Is drug X indicated for a small patient population (less than 7000 in all licensed indications)? YES less than 100 patients
  - Is drug X indicated for patients with a life expectancy of less than 24 months? YES

Abbreviations: BSC Best Supportive Care RCT Randomized Controlled Trial; RWE Real Word Evidence; PFS Progression Free Survival; PPS Post Progression Survival

Case Study from a single arm trial appraisal

Key uncertainties raised by NICE at the 1st and 2nd committee meetings

- ***Not recommended*** - due to substantial uncertainty related to evidence base
- Population in the drug X trials not reflective of clinical practice in England. Trial population had lower burden of disease than English population
- Single-arm design of the trials meant results were potentially biased and trials included few people
- Committee had concerns about the source of the data for the comparator of best supportive care
- Key drivers of cost-effectiveness are the source of best supportive care data, choice of distribution for the survival extrapolation and the choice of progression-free survival utility value
- DH PAS Implemented
- End of Life Criteria met

- Both trials were still ongoing at the time
- Clinical experts and patient experts highlighted that drug X appears to be an effective therapy
- NICE concluded that there was a large degree of uncertainty in clinical evidence but acknowledged that drug X was an effective therapy vs BSC
- Committee concluded that drug X had the plausible potential to be cost effective if its relative effectiveness were closer to the company's estimate than the ERG's.
- Data collection in the CDF would resolve the uncertainty about the effectiveness of drug X when used in clinical practice in England, and data from when ibrutinib was in the CDF could be used to inform a better estimate of relative efficacy.
- ***Recommended within Cancer Drug Fund***

Abbreviations: DH Department of Health; PAS Patient Access Scheme; BSC Best Supportive Care; CDF Cancer Drug Fund