Introduction

Changes to the pharmaceutical regulatory landscape, such as the EMA’s adaptive pathways scheme and the increasing number of medicines developed to treat very rare conditions, has resulted in technologies with smaller or immature datasets at the point of licensing.

Health technology assessment bodies such as the National Institute for Health and Care Excellence (NICE) must therefore issue guidance where there is a more limited evidence base and greater uncertainty in the clinical and health economic case. Since May 2013, NICE has been given the responsibility of determining whether very rare disease treatments (ultra-orphan drugs) should be recommended for NHS-wide commissioning in England. Ultra-orphan drugs are specialised and therefore funded directly by NHS England. In addition, NICE is now responsible for assessing all cancer drugs, to determine those that may be recommended for routine commissioning or made available through the Cancer Drugs Fund (CDF). Managed access agreements (MAAs) are risk-sharing agreements, where the NHS provides conditional reimbursement whilst additional data is collected for new products. We reviewed MAAs included in NICE appraisals and explored trends concerning their design and uptake (Figure 1).

Methods

NICE assessments involving MAAs were identified through online searches. All highly specialised technology (HST), single technology appraisal (STA) and cancer drug assessments to October 2017 were reviewed to ascertain:

- the process under which the MAA was considered
- the key elements of the MAA
- the assessment outcome.

In addition, a review of the NICE methods guides was conducted to understand how MAAs are considered.

Results

MAAs are required for entry into the CDF and are utilised in the assessment of ultra-orphan products via the HST appraisal process.

MAAs may be developed early in the assessment process or following the initial evidence review. Manufacturers of ultra-orphan products are encouraged to consider uncertainties in the evidence and present details of a potential MAA within their HST submission to NICE. A cancer drug can be formally identified for entry into the CDF at three points in the NICE assessment: at submission, during the assessment phase and at the first appraisal committee meeting. There is no formal process for their consideration of MAAs in the single technology appraisal (STA) process.

MAAs generally include:

- a proposal to address the uncertainty
- starting and stopping criteria
- details on data collection, including specific outcomes and time points
- funding arrangements
- financial risk management plans.

Multiple stakeholders are consulted on the details and feasibility of an MAA, and NHS England must agree to the MAA before guidance can be finalised.

In total, nine NICE assessments that included an MAA were identified (Table 1). Of six HST recommendations, three were dependent on an MAA (elosulfase alfa, ataluren and asfotase alfa). Since April 2016, when the new CDF system began, NICE has recommended five products for use via the CDF. To date there is only one example of an STA where the drug was recommended under an MAA. The MAAs relating to the HST and STA appraisals are for a maximum of five years from guidance publication, whilst the timescale for the oncology products is variable and dependent on the timescale for data collection. All schemes include collection of outcome data and include a mechanism to reduce the budget impact on the NHS.

Conclusions

NICE is currently adapting its processes to allow patients access to new medicines at an earlier stage, whilst further evidence is generated.

MAAs that are used as part of NICE assessments in England generate evidence to inform reassessment and limit the financial risk to the NHS, are usually limited to ultra-orphan and oncology products. It is also possible for products not rare enough to meet the HST appraisal criteria, such as belimumab (TA397), to be funded under an MAA, and manufacturers with uncertainties in their evidence should consider this approach.