The Early Access to Medicines Scheme (EAMS): Operational Guidance

Arrangements for Operation across the Medicines and Healthcare products Regulatory Agency (MHRA), the National Institute for Health and Care Excellence (NICE) and NHS England (NHSE)

Operational Arrangements	Explanation / Comments
Purpose	
1. This document sets out how the Medicines and Healthcare products Regulatory Agency (MHRA), the National Institute for Health and Care Excellence (NICE) and NHS England (NHSE) work together to ensure the streamlined operation of the Early Access to Medicines Scheme (EAMS).	A description of the systems in Scotland, Wales and Northern Ireland to be added as appendices to this guidance.
Background	
2. Launched in April 2014, the EAMS aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need. It is anticipated that medicines with a positive EAMS opinion could be made available to patients 12-18 months ahead of formal marketing authorisation. Through this operational procedure, all organisations demonstrate their collective commitment to deliver the EAMS.	
Benefits	
3. Patients in the UK will have earlier access to promising new	

Operational Arrangements	Explanation / Comments
unlicensed medicines before the licence is approved for the treatment of life threatening or seriously debilitating conditions in which there is unmet medical need. 4. Healthcare professionals will have greater confidence in the safety and efficacy of prescribing EAMS products, as the MHRA will issue a positive Scientific Opinion on the benefits and risks of a new medicine. The opinion will provide additional information for clinicians and patients to assist in making a decision on whether to use the medicine before its licence is approved. 5. Companies will gain additional knowledge and experience of these medicines in clinical use. 6. Potential benefits for companies include: • Following the award of a Promising Innovative Medicine (PIM) designation by the MHRA, early dialogue with the NHS and respective HTA bodies to discuss how the medicine will be used in a real life setting and the opportunities afforded to collect further data to inform future decision making. • Scientific opinion assessment with the MHRA allows for full scientific evaluation in advance of Marketing Authorisation. • The opportunity to generate real world patient data in the NHS to further inform value assessment in the Technology Appraisal. • Post Marketing Authorisation, greater evidence and understanding of evidence package for Technology Appraisal approval. • After positive Technology Appraisal, quicker patient access to the medicine based on 30 day implementation.	

Operational Arrangements	Explanation / Comments
7. The MHRA is responsible for regulating all medicines and medical devices in the UK by ensuring they work and are acceptably safe. In the context of the EAMS, the MHRA will provide a Scientific Opinion on the benefit/risk balance of the medicine, based on the data available at the time of the EAMS submission. The Scientific Opinion will be provided following a two-step evaluation process: step I, the Promising Innovative Medicine (PIM) designation and step II, the early access to medicines Scientific Opinion.	Detailed guidance on the Step I and Step II aspects, including fees and contact details, can be found on the MHRA's webpage http://www.mhra.gov.uk/Howweregulate/Innovation/Earlyaccesstomedicinesschemeeams/index.htm
8. The National Institute for Health and Care Excellence (NICE), an Executive Non-Departmental Public Body, provides national guidance and advice to improve health and social care. The Centre for Health Technology Evaluation at NICE develops guidance on the use of new and existing medicines, medical technologies, treatments and procedures.	
9. Fully established on 1 April 2013, NHS England is an Executive Non-Departmental Public Body responsible for overseeing the running of the NHS in England. NHSE directly commissions the prescribed specialised services. It is expected that most of the medicines in the EAMS will be targeted at treatment populations that fall within the NHSE directly commissioned portfolio. As a single national commissioner, rapidly implemented large scale evaluations in the full population can be delivered. In the provision of funds for treatment and hence payment to industry prior to NICE appraisal, NHSE must make decisions that provide equitable access to care and include evaluation	The Manual describes what is part of specialised services - it can be found at http://www.england.nhs.uk/commissioning/spec-services/key-docs/ *Opportunity cost* is the loss of the ability for the NHS to fund other healthcare interventions when a decision is made to apply NHS resources to a particular healthcare intervention. If, for example, a commissioner can only afford to fund one of the following: a cancer treatment, a screening programme, or 6 more palliative care beds then the opportunity cost of choosing the cancer treatment is the loss of the opportunity to fund a screening programme and/or palliative care beds.

of the opportunity costs.	

Operational Arrangements	Explanation / Comments
Operational Procedure	
10. A schematic of the EAMS, including timings and the key points of interaction between the MHRA, NICE and NHSE is shown in Figure 1. The following paragraphs describe the involvement of NICE, MHRA and NHSE at these points in the EAMS process.	
11. **Promising Innovative Medicine (PIM) Designation:** The process resulting in a PIM designation for products is operated by the MHRA. Where a PIM designation is granted, the MHRA will copy this in confidence to NICE, NHS England and the devolved administrations. The company should enter the product details on to the UK PharmaScan database and contact both NHSE and NICE directly, using the contacts provided in the PIM designation letter.	Knowing which products have received a PIM designation is essential to NICE and NHSE to inform horizon scanning, topic selection, topic prioritisation processes, and in building an understanding of the impact costs to the NHS, such as additional activity cost and understanding patient numbers. A timely and effective mechanism is necessary to ensure that NICE and NHSE are informed of which products have received PIM designations. Entry on UK PharmaScan (a single comprehensive database of horizon scanning information for new medicines hosted by NHS Evidence under the auspices of NICE) will help ensure timely sharing of PIM designations amongst the statutory agencies involved in the operation of the EAMS whilst maintaining confidentiality.
12. **Joint Scientific Advice**: The MHRA and NICE strongly recommend that PIM designation holders apply for joint scientific advice. This will be based on the existing scientific advice provision and fees will apply. Following the meeting, the MHRA and NICE will produce separate advice documents to answer the respective questions raised by the	A PIM designation may be granted to a product at an early stage in clinical development and scientific advice can inform forward development, including patient data collection requirements during the EAMS should the product progress to a positive EAMS Scientific Opinion. It is important that scientific advice covers evidence requirements for both

company and will liaise as necessary to support consistent advice.	regulatory purposes and NICE appraisal. This will increase the probability of products introduced to the NHS through the EAMS achieving Marketing Authorisation and having the evidence necessary to support a timely NICE appraisal.
13. **Pre-submission Meeting (PSM):** This meeting, between the company and the MHRA is designed to ensure that all the information needed to allow the MHRA to reach an EAMS Scientific Opinion is available prior to the company formally submitting evidence for an EAMS Scientific Opinion assessment procedure (Step II). To request a PSM, the company completes a PSM template and submits it to the MHRA. The PSM template submission triggers the PSM with the MHRA and an additional discussion between the company and NICE/ NHSE. On receiving the PSM template, the MHRA will contact the company to arrange the PSM and NICE will write to the company to explain arrangements for EAMS medicines at NICE and to set up a meeting with NICE/NHSE.	There are two types of meetings, one with the MHRA and another with NICE/NHSE. The EAMS Scientific Opinion process itself is the responsibility of the MHRA. The Scientific Opinion will be given according to the Step II timetable (either 75 or 90 days), dependent on a positive or negative initial benefit/risk opinion. At this stage, dialogue between the company and NICE and NHSE is critical and is required to ensure readiness of the company for NHS patient access and subsequent NICE appraisal. Discussion areas for NHSE & NICE include: • information requirements in order for NHSE to develop a commissioning policy and to facilitate patient access once an EAMS positive Scientific Opinion is given by the MHRA • anticipated timelines for Marketing Authorisation • current technology appraisal evidence submission plans and how they may be enhanced through data collection in conjunction with the EAMS. Where the EAMS Opinion is based on early data (e.g. Phase 2), it may be necessary for the company and NICE/NHSE to agree plans for data collection (where required) during/beyond the EAMS period to reduce decision uncertainty at the time of NICE appraisal. For example, the NHS England Commissioning Through Evaluation (CtE) model, administered

	by the NICE Observational Data Unit, may be used to coordinate data collection (where required). The need for data collection will be agreed between NHSE, NICE and the pharmaceutical company. Data will only be collected where timescales permit and all parties agree that the additional data collected will add value.
14. **Consideration of NHS Patient Access Prior to the EAMS Period:** The MHRA will communicate a preliminary positive benefit risk conclusion at Day 45 of the step II procedure to relevant stakeholders. Subject to NHSE commissioning policies and processes, including approval by the Clinical Priorities Advisory Group (CPAG), NHSE will make all reasonable efforts to facilitate patient access to EAMS medicines.	The MHRA will inform nominated stakeholders of a preliminary positive benefit risk conclusion at Day 45 of the EAMS SO assessment step. The information provided to stakeholders will be the product name, the company and the proposed EAMS indication. A preliminary negative EAMS SO will not be communicated. Interaction between the company and NHS England in advance of the EAMS opinion (see 9 above) will reduce the elapsed time between a positive EAMS Scientific Opinion and patient access to the EAMS medicine. For example, NHSE will proactively engage with the relevant clinical reference group (CRG) in advance of the EAMS opinion. A positive EAMS Opinion will simplify governance around the use of the medicine. NHS organisations should not duplicate the provision of an EAMS Scientific Opinion at local level in NHS governance and clinical decision making.
15. **EAMS Period:** This is the period between a positive EAMS Scientific Opinion and the Marketing Authorisation. The duration of this stage is expected to be around 12-18 months. The EAMS medicines will be provided to the NHS free of charge by the company during the EAMS period. 16. If no Marketing Authorisation is granted, a company will agree a clear exit strategy with relevant bodies.	The EAMS Scientific Opinion is valid for one year in the first instance and lapses at this time or at the time of the grant of a Marketing Authorisation. Renewal of an EAMS Scientific Opinion should be requested at least 2 months before expiry of the opinion by completing the EAMS periodic updates/renewal template.

17. **EAMS Period (continued):** Where it is identified that data collection at a national scale is needed to support a NICE technology appraisal, NICE/NHS England will consider establishing a Commissioning Through Evaluation (CtE) project. The source of funding for data collection and evaluation (where required) will be agreed during the CtE commissioning process. If NHSE is requested to fund these costs then a decision on access will need to be considered against all competing calls on funding (i.e. including those outside of EAMS).	This is expected to be particularly important for situations where the EAMS Opinion was based on early data (e.g. Phase 2) although there may be important evidence gaps even where the EAMS Opinion was based on Phase 3 data. For some medicines progressing through the EAMS, a CtE project may be unnecessary.
18. **EAMS Period (continued):** Ideally, all relevant EAMS medicines will start the relevant national Health Technology Assessment during the EAMS period to support timely coordination with regulatory processes.	Data collection during the EAMS period may contribute to the evidence available for NICE Technology Appraisal. Also, knowledge that relevant data collection has started and monitoring systems are in place and likely to provide evidence to reduce the uncertainty, may allow NICE appraisal committees to consider recommending the use of promising products in parallel with continued evidence development. This may prove important in achieving timely NHS patient access to important medicines. For an EAMS medicine, subject to delivery of the required submissions and inputs from companies, NICE will schedule the appraisal such that draft guidance (or final guidance in cases where there are no issues requiring consultation) is issued very shortly after Marketing Authorisation.
19. **Marketing Authorisation and NICE Appraisal Recommendations:** NICE issues preliminary recommendations for public consultation or final recommendations (where there are no issues requiring public consultation) as soon as possible after Marketing Authorisation. The regulations relating to NICE technology appraisals (TA) and highly specialised technologies (HST) guidance include funding instructions such that medicines recommended by NICE must be commissioned in line with NICE guidance within 90 days of the NICE guidance publication. For the EAMS products, NHSE will reduce this period	Where public consultation is not required, final NICE guidance will be issued very shortly after Marketing Authorisation and the funding instructions will apply. Access to the EAMS stops at the point of the product receiving its Marketing Authorisation.

from 90 to 30 days. This will include those patients started during the EAMS period. In situations where the final NICE guidance does not recommend a medicine introduced through the EAMS, the company will agree a clear exit strategy with relevant bodies.	

Figure 1: EAMS Schematic