Early access scheme – consultation

Response from the UK Medicines Information Service (UKMi)
October 2012

Question 1: Do you consider that a scheme that makes available in the UK certain new medicines before they are granted a marketing authorisation (licence) will be of value to patients?

Earlier access to medicines that meet the criteria specified will undoubtedly be of value to some patients, particularly those who have run out of therapeutic options. Compared to existing named patient/ patient access schemes, the proposed scheme has the potential to increase the number of patients who may receive a treatment prior to licensing. The proposed scheme has the added assurance that a review has been carried out on available data by an independent body.

We appreciate that medicines will have to demonstrate a favourable risk-benefit profile before they can be supplied via this scheme. However, giving early access to medicines that have not been fully assessed will undoubtedly increase the risk to patients. The medicine may not be as effective as the data initially suggest by 'rapid' review, and safety will not have been fully assessed, increasing the potential for patient harm. Patient safety must be paramount. It is essential that patients are aware of the risks and understand the implications of using a medicine that has not has not gone through the approval process. The risk to the clinician is also increased; available information for decision making will not be comprehensive and liability is an issue when prescribing an unlicensed medicine. There are also risks for organisations; use of unlicensed medicines increases administration costs associated with record keeping and individual dispensing requirements for example.

The scheme could introduce inequities. Uptake of medicines available through the proposed scheme could vary based on decisions of local commissioning organisations to fund unlicensed medicines. This could have a negative effect on patient care.

The scheme could provide significant patient benefit if it were used to provide 'real world' data between the period of the end of the clinical trial programme and full regulatory assessment. This could take the form of a patient registry. It is essential that safety data be actively collated from patients receiving medicines via this scheme; collection of efficacy and safety data would provide the greatest benefit. Patients treated during this period may be more representative of those seen in practice than patients enrolled in clinical trials. Having this data available for the marketing authorisation assessment may help resolve issues that clinical trial data are unable to.

An important consideration for this scheme is that adequate supplies of the medicine must be available to meet the demands generated and that the supply chain is not too onerous for healthcare providers.

Other concerns that may need to be addressed include patient self-funding and whether the scheme could promote EU health tourism.

Question 2: Do you have views about the scope of the proposed scheme (for example the type of illnesses and conditions that will be included)?

The proposed criteria for medicines eligible for this scheme are sensible. We do not think that the scheme should be limited to a particular kind of illness or condition.

Question 3: Do you consider that our assessment of the likely number of medicines per annum to which the scheme will apply is accurate? If not, why not? What do you consider might be a more accurate assessment of the number of medicines to which the scheme might apply?

We think that up to five medicines a year may be eligible for this scheme, but as there are other EMA and MHRA schemes available, the number of applications will depend on how the pharmaceutical industry views the benefits of this scheme versus the others. The impact of this scheme could be negligible if few medicines qualify or are submitted for inclusion.

We note that there is a similar scheme in France that has been running for several years, and the number of applications for this has dropped recently.

Question 4: Do you have views on the proposed stage of development of a medicine that this scheme will be available?

We agree that limiting the scheme to those medicines that have completed PIII clinical trials has the advantage of ensuring that there will be sufficient data on which to make a benefit:risk assessment. The scheme must not interfere with recruitment into clinical trials that are necessary to provide the data for full regulatory assessment.

We consider that clinical trials for medicines eligible for this scheme should have used validated outcomes and/or followed EMA guidance in terms of study design, population and outcomes for the disease, if these are available. As EMA guidance/ validated outcomes may be lacking in areas of unmet medical need, we think it preferable, in these circumstances, that medicines eligible for the scheme should have been studied in trials that have incorporated patient orientated and quality of life outcomes.

We note that in exceptional circumstances some medicines may be considered for the scheme based on PII data. At this phase the intended population and the dose may not have not been defined and many medicines undergoing PII studies do not make it to the market. Where unmet need is significant there may be benefits to considering medicines at an earlier stage in the lifecycle, potentially after PIIb studies. Medicines unlikely to progress through PIII studies, for reasons such as the rarity of the disease, may be considered for the scheme. The risk of making medicines available without PIII data may be mitigated to some extent, if the application is for a licence extension of an already approved medicine, rather

than for a new medicine. In these circumstances, the risk profile of the medicine, albeit in a different population, is clearer.

Question 5: What do you think should happen to patients receiving treatment with a medicine under this scheme if the medicine subsequently fails to be granted a marketing authorisation?

The outcome might be different if the medicine failed to gain market authorisation on the basis of inadequate efficacy or on safety. If the EMA/MHRA required a further study before a decision on marketing authorisation could be made, new patients should not be recruited into the scheme but into clinical trials. Access to the medicine under the scheme might be continued for existing patients if they had gained clinical benefit from treatment. Patients must of course be fully involved in the discussion about whether to continue treatment or not. However, it is unlikely that commissioning organisations would fund a treatment that had failed to gain marketing authorisation.

If a medicine was not granted marketing authorisation, continued supply could be additionally be jeopardised as the company may stop manufacture.

Question 6: What information would patients, clinicians other than healthcare professionals want MHRA to publish on the website when a medicine is given an opinion under this scheme?

In addition to the information specified (an opinion, a summary assessment report and a summary of product characteristics) it would be useful to have detailed treatment protocols agreed with MHRA that clearly define which patients are eligible for access to the medicine under this scheme. The assessment report should include a clear explanation of areas of uncertainty and where data are lacking. This might include the questions that the MHRA had formulated during the review that would have required clarification from the company during a full assessment. These should be in a format suitable for both healthcare professionals and for lay people.

There should be a clear explanation of the scheme, what it means for the patient, and what might happen if the medicine does not gain marketing authorisation.

The risk management plan should be published. Details on how and where clinicians and patients can report safety issues and adverse reactions should be available. Quarterly updates of reviews of safety while the medicine is available through the scheme would be valuable.

Question 7: What information about the medicine would be useful for MHRA to publish on the website for use by clinicians, other healthcare professionals and those making decisions about funding?

Information that is normally provided by companies to commissioners prior to marketing would be useful for medicines accessible via this scheme. This

information would include estimates of the burden of disease and treatment options available.

Information on the supply process for the medicine via the scheme would also be useful. Links could be given to published information, including any economic analyses, and to documents from other regulatory agencies if the medicine is licenced abroad.

Details of any restrictions on who can prescribe the medicine, or the competencies required if this is an issue, would also be useful.

Information more appropriate to a restricted access resource could be relayed via other websites such as UK Pharmascan. NHS organisations need to plan for medicines that will have an impact on their budget or services, so an indication of which medicines are being assessed for this scheme is essential. In addition, estimates of potential uptake could help with planning, as would a regularly updated forecast on when the medicine might achieve marketing authorisation.

Question 11: Please provide an assessment of which of the 5 options (a-e) you consider would be best able to meet the requirement that NHS funding must be cost effective, most likely to most likely to ensure equity of access for patients and most acceptable to stakeholders (especially industry, patients, the NHS, NICE).

A full cost-effectiveness review would be the ideal, but in our view is not achievable within the timescale. If an economic analysis had run alongside PIII studies, a review of this analysis by NICE would be valuable. The lack of a cost-effectiveness analysis will be a major concern to commissioners trying to prioritise this medicine against other competing demands and could impact on uptake.

We agree that cost-effectiveness is guaranteed if the medicine is provided free of charge and this is generally the case for medicines made available through compassionate use or patient access schemes. Like these schemes, the early access to medicines scheme will increase the burden on the NHS in terms of managing the scheme, collecting data and potentially increasing use of diagnostics and disposables. In relation to this we consider that the company should fund any specific testing required, eg for gene mutations, prior to full marketing authorisation.

We do have some concerns about this approach. The scheme itself may result in larger numbers of people receiving a medicine prior to market authorisation than existing schemes. This compounds the ethical dilemma faced by NHS commissioners when the medicine is licensed in having either to find the funding to allow continued treatment or to discontinue treatment. If the medicine displaces an existing treatment, the NHS has to find completely new money to fund the medicine having already made the savings from those medicines it has displaced during the early access phase.

For these reasons, there is some merit in considering option b, which suggests that the cost of the medicine would be capped at the cost of the treatment for which it directly substitutes. In areas of unmet medical need, this may be an

issue. Also, the new medicine may be used in addition to, rather than as a substitute for, existing treatment. If this option were to be utilised, we believe NICE should be involved in the verification/decision of the level of funding this might involve. This approach has the advantage that the NHS is still funding treatment for the disease and if the medicine is marketed at a higher price following value-based pricing, the difference in cost to the NHS will not be as great as it would if the medicine had been provided free of charge. In addition, there would be less chance of a perverse incentive to over use the new medicine and its use would be cost-effective for the NHS.

Having said that, there is real concern about the burden that this scheme will impose on NHS practitioners and commissioners. Although 'ring-fencing' has been discounted there is a case to be made for establishing an 'innovation fund' generated by the NHS and the industry that can be used to support this scheme if it progresses. Such funding could support the collection of data needed to ensure that this scheme benefits patients in the longer term.

Question 18: What information (in addition to the scientific opinion - see question 6) would patients and clinicians find helpful in deciding about treatment with these medicines?

Some of the information we have suggested in our responses to questions 6 and 7 may be relevant here. In addition, we think that it would be valuable to have MHRA approved patient consent forms to be used for medicines made available under the scheme readily accessible so that patients may read them in their own time ahead of making a decision. Decision aids for patients to help them weigh up the benefits and risks would be extremely valuable.

A clear statement on liability, for both patients and clinicians would be helpful.

Question 19: How could such information best be presented?

Decision aids for patients could take the form of 'smiley face plots' as found on Dr Chris Cates' website: http://www.nntonline.net/

Question 21: What do you think will be the most likely constraints in uptake of this scheme (eg bureaucracy, uncertain NHS uptake, cost of the medicines)?

The problem with existing schemes is that uptake is uncertain. This also applies to this scheme. Cost-effectiveness will not be clear and uptake could be patchy making it unattractive to the industry.

A full safety assessment normally be achieved through the regulatory process will not be available. This, together with the unlicensed status of the medicine increases the liability of clinicians and organisations.

Elements of the potential increased burden on the NHS have been highlighted elsewhere.

Question 24: Do you have any further comments to the content of the scheme that have not been addressed by your previous answers?

Would prescribers need to be registered/ certified to use medicines provided under this scheme? Will there be sanctions in place if the prescriber fails to collect required efficacy or safety data necessary for the scheme?

Finally we would like to stress the risks to patients around safety, and the aspect of inequalities this proposal may introduce. In addition there is a risk that commissioners may be forced to remove funding from existing evidence-based treatments to the unlicensed ones proposed in the scheme.

There is insufficient evidence provided within the consultation that this scheme would have economic benefit for the UK.