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The Royal Pharmaceutical Society (RPS) is the professional body for pharmacists in Great Britain. We represent all sectors of pharmacy and lead and support the development of the pharmacy profession including the advancement of science, practice, education and knowledge in pharmacy. In addition, we promote the profession's policies and views to a range of external stakeholders in a number of different forums.

Its functions and services include:

Leadership: representation and advocacy: promoting the status of the pharmacy profession and ensuring that pharmacy's voice is heard by governments, the media and the public.

Professional development: education and support: helping pharmacists to advance their careers through professional advancement, career advice and guidance on good practice.

Professional networking and publications: creating a series of communication channels to enable pharmacists to discuss areas of common interest.

Thank you for the opportunity to comment on this consultation. We would like to make the following general points which address the proposals from a pharmacy perspective. We have not answered all the consultation questions as some of these are outside the remit of a professional body.

General Comments

Patient safety is at the heart of all pharmacy practice. The RPS is working to make Great Britain the safest place in the world to take medicines and recognises the need to have robust licensing and approval processes in place which must also be fair, transparent and timely. We are supportive of the founding principles of the NHS: "to offer free medical care to the entire population" based on the patient's clinical need and fair and equitable access to evidence based medicine for all. However, access must always be balanced by the need for patient safety and the current governance procedures which ensure safety and efficacy should only be circumvented in very exceptional cases. Having a marketing authorisation (MA) is fundamental in this process.

From the information in the consultation we are unsure of the requirement for an addition to the access options currently available, in particular the named patient route. Clarity is required for clinicians on the existing ways of early access. We believe there would be merit in collating

and simplifying the current alternatives to give clinicians clearer guidance on which options would suit individual patient needs. Shorter timescales in processing applications using existing options would be one of the most efficient ways to speed up patient access.

We note that the MHRA is already committed to an early access scheme and therefore this consultation is not requesting comments on the introduction of a scheme but on the detail of the proposals themselves. In addition the proposals will not enhance equitable patient access across the NHS as individual health boards and PCTs will still be responsible for deciding whether or not to fund any medicines given a positive opinion under the proposals.

Pharmacists work in many different areas of healthcare and can specialise in a variety of therapeutic areas including clinical trials and medicines governance. They are healthcare professionals with a unique training and expertise in all aspects of medicines and we therefore suggest that whatever the final outcome of the proposals, pharmacists are consulted and have strategic input at an early stage. Pharmacists also have a role in providing expert and impartial advice to both clinicians and patients on the evidence base, the risk benefit balance, and the liability and responsibility issues when using unlicensed medicines.

Consultation Questions

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?

In principle ,yes ,such a scheme could be of value for a small a cohort of patients for whom the benefit: risk ratio is such that they might benefit from early access to a medicine, however , very clearly, the earlier introduction of medicines prior to gaining an MA also carries an additional clinical risk . Since the majority of prescribing within GB is within the NHS, and is therefore dependent on NHS funding, the NHS will wish to ensure the safety and cost effectiveness associated with medicines use as an area of high spend. Prescribers are also understandably cautious when prescribing new medicines so it is difficult to predict how many patients would ultimately benefit from the new scheme.

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)?

Acute conditions with finite courses of treatment will be simpler to administer. Treatment of long term conditions could cause problems for patients if decisions not to approve were taken at a later stage by the National Institute for Clinical Excellence (NICE), Scottish Medicines Consortium (SMC) or the All Wales Medicines Strategy Group (AWMSG). Given the increased risk with early access this route should only be used in exceptional circumstances e.g. where there are no other adequate treatment options or all available treatments have failed. If the proposed scheme is introduced there must be a straightforward process that does not deter prescribers, health authorities and suppliers from obtaining medicine for patients.

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?

The retrospective figures MHRA has supplied in the impact assessment are as accurate as estimate as possible at the moment. Truly innovative breakthrough medicines are less common than class variations for similar indications but innovation in treatment is rapidly advancing in areas such as biologicals and it is difficult to predict future numbers with any accuracy.

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

From a patient safety perspective access applications after phase III trials should be the earliest to be considered. Numbers of patients in phase II trials are very small and therapeutic doses have not yet been established. Some medicines fail to gain a MA after phase III trials and more information on the number of failures at this stage would be useful to build confidence in the proposals. Many more however do not progress from phase II to phase III and some do not successfully complete phase III. Therefore potential patient safety issues after phase II should take priority over early access.

Adverse events do not always come to light until medicines are being used by very large numbers of patients. There are many historical instances of medicines withdrawal for serious adverse events after global marketing and in phase IV trials.

Whenever possible access to medicines after phase II should be by inclusion in a clinical trial, however we appreciate the narrow criteria used for admittance to most clinical trials will exclude some patients and therefore there might be very exceptional situations where a patient might benefit. In these circumstances patients would require to have clear guidance on the risks involved, the lack of knowledge on definitive benefits, where liability lies and the experimental nature of the treatment compared to normal routes.

We are not clear where the advantage in an early access scheme after phase II would lie compared to supply on a named patient basis given the exceptional patient safety issues which must be considered.

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?

This would be no different to the current situation when a patient is doing well on a clinical trial but the medicine subsequently fails to gain an MA and is unavailable or NHS funding is not forthcoming. A clear exit strategy must be a requirement of an early access application. Patients need to be fully aware of the potential limitations of treatment and timescales agreed. Inevitably, there will be patient distress if successful treatment is terminated due to lack of funding or non issue of an MA. Clinicians would require to use another method of access such as Compassionate Use or Named Patient Supply as appropriate. There will be pressure exerted to continue prescribing which will impact on NHS budgets. This must be weighed against benefits for the majority of patients in more general cases.

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?

- As much patient safety information as possible in an easy to understand format.
- Information on how complete the data was compared to the usual MA applications and any significant tests/ data missing.
- Any Significant Adverse Events already known and the incidence of them.
- Clear guidance on the liability and responsibilities of all parties.
- Information about the trial sponsor and the Clinical Research Organisation managing the Clinical Trial.
- Information about any Compassionate Use Program or Named Patient Program for the medicine and which organisations are managing these programs.
- For medicines that are already licensed in other countries all patient information and summary of product characteristics should be available in English.

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?

- The scheme and how it operates should be fully transparent to healthcare professionals.
- As above (Q6) but with more statistical and detailed information available for those able to interpret it as well as financial details.
- Any information from other countries where licences had already been granted and the licence indications would be useful.
- Financial details of costing

Question 8: How much will the impact of monitoring and surveillance arrangements influence your company's decision to use this scheme?

No comment.

Question 9: Please estimate the cost per medicine of setting up a likely surveillance package and appropriate Risk Management Plan (RMP).

No comment

Question 10: We assume that as most of these medicines will go on to be licensed the need to develop a surveillance package and RMP will not be a critical factor in a decision to use this scheme. Is this correct? If not please explain why not.

No

We believe ongoing surveillance would be essential as risks will emerge with continued use which will not yet have been picked up in the trial phases and pharmacovigilance arrangements must ensure the ability to respond quickly should problems arise. The black triangle and yellow card schemes could be extended to highlight these early access medicines and the greater risks associated with their use. As above we would like more information on

the numbers of licence applications which are turned down and the rationale for these decisions.

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 ensure equity of access for patients and most acceptable to stakeholders (especially industry, patients, the NHS, NICE).

A combination of capping and free pricing (b and c) would ensure no extra costs were incurred in the NHS but capping is an artificial ceiling. It does not increase public and patient confidence when prices are adjusted purely to gain NHS funding, indicating overpricing in the first instance. The criteria for funding is well established. Companies should apply stating the cost they are actually prepared to charge.
This statement excludes the consequences of any future implementation of value based pricing which would affect all drugs and not adversely affect confidence in one company in isolation.

Question 12: Are there other approaches that we could have included here? Please describe.

No comments

Question 13: Please comment on the assumption that whilst the options that include an element of NICE review will incur costs, these will simply advance those costs as the information required will also be required for a later full NICE review.

This is for NICE to answer

Question 14: Can you quantify likely costs of the limited NICE reviews described here?

This is for NICE to answer

Question 15: Which of the options described is most likely to meet the requirement that this scheme must deliver economic benefit for the UK?

This question is outside the remit of a professional body

Question 16: Can you provide details of any other approaches that could be considered?

This question is outside the remit of a professional body.

Question 17: Do you have any comments on the assumptions made in these options?

No comments

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?

Patients would require information in the usual way when a new treatment is considered giving an overall assessment of the options available and the risks and benefits of the treatment. Patients are often prepared to take risks for example a clinical trial, when the results will be examined and followed up, not only for their own benefits but for those of others and when there are no alternative treatments available. The distinction between a clinical trial and the early access scheme would need to be clearly defined and explained. Any available information from other countries should be made available in English.

Question 19: How could such information best be presented?

Discussion with the patients' clinician would be essential .Guidance from the regulator would be useful .This could be printed out after discussion for patients to consider in their own time. Information leaflets alone are not enough as patients will rely on their clinician's professional opinions Medicine sponsors usually have information manuals and the regulator should permit that these are shared with patients as currently it is not clear what type of information is able to be provided to clinicians and patients.

Question 20: Do you have any comments on the proposed charges under this scheme?

The suggested proposals seem fair and reasonable and a cost effective alternative to a full European approach, although equity of access across the EU would be the ideal outcome.

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

Patient safety aspects will be of prime concern along with cost effectiveness and lack of evidence base. Paucity of data on patient outcomes will be a strong consideration as there needs to be a strong argument for patient benefit to warrant prescribing, even in extreme cases.

Question 22: Is this scheme likely to be more or less attractive than other schemes that currently offer early access to medicines (these are set out in the accompanying Impact Assessment and in the list recently published by the MHRA at:

http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Regulatoryschemesthatsupportdrugdevelopmentlicensingandpatientaccesstoinnovativetherapies/index.htm
If so why?

The impact assessment states that there is a lack of knowledge about current schemes. Would information about this scheme be more widely available?
Given the small numbers of drugs liable to be used the scheme, we are not clear on how advantageous it would be over other schemes. Clearer guidance on the schemes currently available for prescribers on the most suitable routes for individual patients would be helpful. E.g. a table showing comparisons/ advantages /disadvantages/FAQs.

Question 23: We understand that schemes in the US that offer early access to medicines are used more extensively than those available in the EU. Is this correct and if so why?

Anecdotally we imagine that the wide variance between the US and UK healthcare systems would influence take up. The majority of patients rely on NHS funding in the UK as opposed to insurance company funding in the US.

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

We envisage the supply of early approved medicines to be through specialist hospital physicians and hospital pharmacies only and subject to the processes and procedures currently in place for any unlicensed or NICE/SMC non approved medicines. As the experts in medicines, pharmacists must be included in the governance of any access scheme.

Currently the criteria used for clinical trials does not reflect the real population and if a model could be found ,as in Option b section 40 of the consultation ,to have access as a 'real world' arm of a clinical trial this could be an appropriate solution to many of the issues under discussion.

MHRA is the regulator for GB and it is therefore disappointing to note that all references in this consultation are to NICE with no mention of the other organisations in the devolved countries such as the SMC or the AWMSG.
Kind regards,

Mair Davies	Shilpa Gohil	Prof. John Cromarty
Chair	Chair	Chair
Welsh Pharmacy Board	English Pharmacy Board	Scottish National Board