****

**Validating the UKMi medicinal products risk assessment tool**

**A summary of process, responses, and actions**

1. **Background**

Following discussion with staff in NHS England, UKMi worked with patient safety and other specialist pharmacists to develop a tool aimed at aiding prospective identification of patient safety issues associated with individual products for medicinal use before their introduction to clinical practice. A development group met a number of times to work up a comprehensive version of such a tool (presented as an excel spread-sheet) as well as an abbreviated version (presented as a PDF). The abbreviated and full versions are designed to sit alongside each other, such that the abbreviated version provides a screening step prior to use of the full tool.

The development group felt that prior to any introduction to practice, the resources required a process of validation. This paper describes such a process and its outputs

1. **Validation process**

The validation process followed a number of distinct steps outlined below.

1. **Validation scenarios**

The development group worked up three hypothetical (but practice-based) testing scenarios that were deemed appropriate to validate the tool.

The first concerned Retacrit (epoetin zeta) a licenced product for which the use was described as being within the licence for the purpose of the scenario. The scenario suggested that a Trust was considering switching from epoetin alfa to Retacrit because of comparative cost; however, such a switch may have posed issues given the packaging of the new product and health professional familiarity with it.

The second scenario considered a range of artesunate products; all of these were unlicenced and being used for *falcipurium malaria.* The products were in-fact pharmaceutically identical (all being from a single Chinese manufacturer) but differences in presentation (due to differences in over-labelling and packaging from different foreign pharmaceutical companies) meant that they presented different risks.

The third scenario concerned the use of bupivacaine, 0.25%, 20mL amps; a licenced product. The scenario concerned the use of the product intra-pleurally following thoracotomies. There is some ambiguity as to the licensed status of the product for this indication and particular concerns as to whether the product is suitable for such a use.

1. **Validation approach and questions for validators**

Medicines safety pharmacists and their teams within Trusts were used to validate the tool using the scenarios above. The process did not seek to objectively validate each component of the tool against a known set of responses; instead the scenarios provided a mechanism by which subjective feedback could be gathered from individuals about the tool’s usefulness in practice. The reasons for pursuing the more subjective approach outlined were firstly that each hypothetical scenario may have raised different patient safety considerations for individual organisations; and secondly, that the number of validators and the capacity to process their responses was limited. Hence responses in relation to each scenario may have varied greatly, with the number of respondents being too few to enable the cross-checking that would have been necessary to pursue objective validation. In addition, subjective validation informed by expert responses was deemed appropriate given that the final the tool is intended as a pragmatic resource at point of use rather than an academic or regulatory product.

Ten medicines safety pharmacists were emailed all of the testing scenarios mentioned above, an explanatory letter, and the draft tool in both abbreviated PDF and full spread-sheet versions. All documentation associated with the validation is available on request. Validators were asked to complete as many testing scenarios as they were able, to provide comment on the general usefulness of the tool in helping them think through the medicines safety issues raised, and to feedback specifically on the following questions:

* How long the process took, using either the PDF or Excel version of the tool?
* Whether the tool helped establish patient safety considerations that might not otherwise have been considered?
* Whether there were any significant patient safety themes in relation to medicinal products that have been missed?
* Whether there is any unnecessary repetition in the tool? Since ideally each of the questions should provide a unique insight.
* Whether they felt that, overall, the tool provides a useful mechanism by which to prospectively identify patient safety considerations related to the use of new medicines?

1. **Processing of validation responses**

Validation responses were processed by Ben Rehman, Director, London Medicines Information Service, with support from Trevor Beswick, Director, South-West Medicines Information Service. Processing validation responses led them to being broadly categorised as being of 3 types:

* general comments about the tool, particularly in relation to the time it took to use and the overall usefulness of the approach suggested;
* comments about specific existing components of the tool, and whether they require further development;
* comments about particular patient safety aspects related to the first time introduction of a new medicinal product which are not covered in the tool currently, but which the tool should consider addressing.

1. **Results of the validation**

Nine responses were received from the ten medicines safety pharmacists emailed. In some instances, responses were not from the individuals who had originally been contacted but were from members of their teams at a variety of grades and roles. Whilst this was not the original intention it was in fact deemed to enrich validation since ultimately the tool is intended to be applicable across a wide range of roles, grades, and practice settings.

As outlined above, comments from validators can be broadly grouped under 3 categories.

1. **General comments about the tool: time spent using it and its overall applicability**

The time spent using the tool for each scenario varied significantly: some validators reported that they had spent half a day working through a single testing scenario with the tool, whilst others reported that they had spent 2-3 minutes working through the same scenario. The median time for each validator was around 30–60 minutes per testing scenario.

Validators’ views on the usefulness and potential applicability of the tool were, almost universally, positive. They typically said that the tool was comprehensive, that it picked up many of the issues that they would have expected it to, and that it brought together well different pharmacy considerations in relation to the safe introduction of new medicines (i.e. it enabled procurement, clinical, medicines information, and quality assurance aspects to be considered in the same place). There was an appreciation that the comprehensive nature of the tool was unique, and that providing the tool has the potential to improve consistency. Validators suggested that such improvements in consistency might relate to ensuring a safety assessment is always conducted at some point prior to a medicines’ introduction, ensuring such assessment is completed in a similar manner regardless of the assessor or where in the health-system it is conducted, and in ensuring that appropriate management plans exist where problems are identified.

Respondents were also in the main positive about the presentation of the tool. They suggested that although long (particularly in its full version) the presentation provided them with a well-structured mechanism of establishing patient safety considerations and of documenting these in a consistent manner. A number of respondents noted that as they gained familiarity with using the tool the time it took them to complete testing scenarios decreased. There were mixed views on whether the initial screening and fuller versions dovetailed together adequately and whether one or both were necessary; however, the general view seemed to be that making both available and allowing individuals to decide the level of detail they required is appropriate.

1. **Validators’ comments on specific tool items and whether they require further development**

Validators made a number of specific comments on individual tool components and how these could be further refined and improved. These comments are tabulated below, together with the actions that have been made both for the full (Excel) and abbreviated (PDF) version of the tool.

| **Tool item** | **Validator comments (précised where appropriate)** | **Action for full version** | **Action for abbreviated version** |
| --- | --- | --- | --- |
| A5 | One validator suggested that this is split up so that the need for technical and patient information is covered separately. | Test the suggestion with the development group, but I think probably it is adding an unnecessary extra question splitting this up. | As per full version. Any amendment for the full version will also need to be made on the abbreviated version. |
| C4 and F6 | One validator suggested that there is a potential overlap between these elements and that they could be rationalised and combined as one question. | This seems a valid point. I think it would be best to cover all this in the “information provided with the product section” and so have made the appropriate amendment to item C3. | Similar amendment made for the abbreviated version. |
| D4 | Agreed with the concept of including prescriber familiarity, but wondered whether the wording conveyed the appropriate meaning. Suggested that in local practice the following has been used to address a similar issue:  *For the expected population, is the pathway of care such that it might lead to prescribing of products unfamiliar to prescribers?* | Test the suggestion with the development group; the revised wording is perhaps clearer in covering the same point. | Any amendment for the full version will also need to be made on the abbreviated version. |
| D5 | Considered that this element should be split or should otherwise be re-done to ensure the particular issues related to paediatrics are drawn out. | Test the suggestion with the development group, but overall I think the paediatric point is already covered in the associated guidance notes. | There are no guidance notes for the abbreviated version, but I’m still not sure we need to pick this up specifically as it is reasonably clear in the full version. |
| F4 | Add either here or in section J that where manipulation is required, the environment in which that occurs might have a bearing on the safe use of the product. That is, an environment conducive to safe manipulation needs to be present. | This seems a valid point that should be covered in the tool. I have suggested the following:  *Where the manipulation of the product is complex, is the environment in which it is to be prepared conducive to safe use? That is, will it be as free as possible from distractions and is it an otherwise suitable environment for complex manipulation?* | As for full version, include this additional question. |
| G4 contd | Validators suggested that for this element, the question should be split into two for clarity since whether monitoring is required and whether such monitoring is achievable are two very different things. | This seems a valid point. I have split the question. | Not really possible to split up in the abbreviated version any further although they are separate questions already. |
| K2 | A number of validators discussed that this question needs to be split up into two components. That is, the penultimate question should be about whether there are risks identified in relation to the status quo. And the final question should be about whether those risks are the potential benefits against alternatives. | This seems a valid point. The next version of the tool has been amended to reflect this suggestion. | As per the full version. |
| All components | Two validators suggested that for some of the components “not applicable” boxes were required, particularly in the abbreviated tool. They suggested that B4 and B6 should include these. | More applicable to the abbreviated version. | I don’t think this really needs addressing. I think we got the “not applicable” element about right first time round, and there is always the comments box if people don’t feel they need to complete a particular component. Discuss with development group at the next meeting. |

1. **Validators’ comments on additional items that the tool could cover**

In addition to providing specific responses on the tool elements that exist currently, validators also suggested a number of themes and areas they felt should be further developed as well as providing comment on how the tool could be used in practice. Taking all these potential new features forward will require discussion with the development group, but the points raised were as follows:

* Should the tool include a question in relation to whether additional labels and warnings are to be applied to products?
* Should the tool better cover excipients and any changes to these? In particular, could the presence or otherwise of phenylalanine, sugar, or alcohol be added as a question since these have potential consequences in specific patient groups.
* Where IV products are being considered, could the tool make better reference to the NPSA risk rating tool in NPSA patient safety alert 20? [Note: this the NPSA 20 work was considered in some detail by the development group previously].
* Should the tool make specific reference to compliance with the safer sharps initiative? That is, should the tool specify that new injectables should be safety-engineered devices that will retract, sheeth, or blunt immediately after use?
* Should the tool incorporate never events in some way?
* Intelligence as to the environment, users, and practical aspects related to the product’s use are often the more difficult components to establish and quantify. Maybe there could be some more provided in relation to how these things can be established and how any issues that are identified can be addressed?
* Could the tool better cover the situation in relation to COSHH and medicines? And is the current question in relation to COSHH appropriate since COSHH may not apply to medicines? [Note: our understanding when developing the tool was that COSHH applies in relation to operator safety when medicines are being prepared, which is how the question is phrased]
* Could it be clearer as to how this is to be used? In particular, what elements could or should be completed by Trusts, and what elements might be completed prior to Trusts seeing the medicine?
* As well as using this as a mechanism to identify the issues, the tool could also be used to help start thinking through mitigating steps. Could a final RAG, risk rating, or some other scoring system be used in the tool? This would then allow the development of mitigation plans.

1. **Summary and options for implementation**

In summary, the validation process pursued was largely successful and as such suggests that the tool is fit for its intended purpose of systematically and prospectively identifying potential medicines safety concerns as products are introduced to practice.

Validators provided useful comment both on specific tool items and on areas for potential future and further refinement. As specified above, particular refinements have been made now to the tool (where those are clear cut) but there will also be a need to continue the process of ensuring the tool remains useful. To do this, it will be important to maintain the oversight structure we set-up for the tool’s development, and we would suggest that the national development group chaired by UKMi remains in place as we implement the validated product.

UKMi remains committed to this work, and has thought through a number of options in relation to the NHS implementation of the tool. We would welcome a discussion with the NHS England Medicines Safety team about the best way forward with the tool, both in an NHS context and as has previously been discussed, in relation to pharmaceutical industry and regulatory standards. Options for NHS implementation of the tool include the following:

1. The tool is made available across the NHS for all to use, with UKMi continuing to develop the tool but with little other input

In this option, the tool is made available across the NHS for any pharmacist or other professional involved in medicines safety to use locally where they deemed that appropriate. This option has advantages in promoting the prospective identification of medicines safety issues local, but it also has some potential drawbacks in relation to the optimum use of the tool. Particular concerns might include the large variation in responses that might occur between practitioners without any process of quality assurance, the duplication of effort that might occur given the limited co-ordination that would exist, and the limited ability to pick-up new products as they were marketed given that this could not easily be linked to horizon scanning processes.

1. UKMi applies the tool to all new products only and publishes the results, without making the tool itself widely available

In this option, the tool would be a device that was pinned to the existing new medicines horizon scanning work of UKMi. The model would be that as the development of new products is identified by UKMi, the tool is used to produce a summary of medicines safety issues that could be built into existing outputs and which would help inform safe introduction. A repository of such evaluations would be established.

The model would have a number of benefits: in particular that the quality of the assessments using the tool could be reasonably assured and that new products with potential medicines safety issues could be identified early, potentially sometime before their launch. However, the model would not allow use of the tool to be responsive to very local problems, and it would also not easily allow identification of medicines safety issues related to unlicensed or off-label uses since these would be outside current horizon scanning. In addition, it is unlikely that UKMi would have the capacity to consider anything other than new medicines, and so changes related to introduction of a new product for other reasons (for example, as a result of a procurement decision for an existing generic medicine) would not be able to be picked up easily either.

1. A mixed model: UKMi applies the tool to all new products and publishes the results, but also facilitates other local and pan-regional use of the tool

This option requires further development, but it is probably the most viable and potentially useful for the NHS.

Here UKMi would establish and maintain a repository of medicines safety evaluations for new medicines, with these pinned to existing horizon scanning processes broadly as described in option 2 above. In addition, however, UKMi would work with procurement, quality assurance, and medicines safety colleagues within specialist pharmacy services; as well as with medicines safety networks to encourage use of the tool. Particularly in relation to medicines safety networks, UKMi would provide a quality assurance function for the medicines safety product assessments such that completed assessments could be published on a nationally available electronic repository.