

FMEA: a new approach to manage high risk medicines

A prospective risk analysis tool, failure modes effects analysis (FMEA), has been used by a pharmacy team at Northumbria Healthcare NHS Foundation Trust to improve the safety of rituximab use. This article describes the benefits and challenges of using the FMEA method. By Steve Williamson, Nicola Wake and Gemma Donovan.

Reducing harm from high risk medicines, including injectable medicines and cytotoxic chemotherapy, is a key priority for the NHS (see background box).

At Northumbria Healthcare NHS Foundation Trust, pharmacy and nursing staff are familiar with handling and managing traditional cytotoxic chemotherapy drugs and many safeguards have been put into place. However, the recent introduction of a number of new, biologically targeted anti-cancer therapies, in particular the monoclonal antibodies, has posed new safety challenges.

The NHS Pharmaceutical Quality Assurance Committee recommends that the manipulation of monoclonal antibody preparations should be individually risk assessed, and those with high risk should be

manipulated in pharmacy aseptic facilities.⁵ In cancer services it is normal for nursing staff who are trained in chemotherapy to administer these drugs under written protocols, with close monitoring. However, the demand for the administration of these drugs outside of cancer services raises new safety considerations. For example, where prescribing volume is low, nurses may not be trained or may not have the resources for the high level of monitoring that these treatments require.

This article describes a pilot project to highlight the risks associated with the use of rituximab (Mabthera; Roche) and thus identify areas for improvement. Although use of this drug is well established in the Trust, its use is increasing as it gains approval for different indications.

Background

In 2007, the National Patient Safety Agency (NPSA) issued a report entitled 'Safety in doses: improving the use of medicines in the NHS'.¹ This report, recently updated (September 2009), describes the problems related to medication errors and how NHS organisations and healthcare staff can improve patient safety by identifying areas of particular risk.

The same year, the NPSA published an alert entitled 'Promoting safer use of injectable medicines'.² This report stated that the incidence of errors in prescribing, preparing and administering injectable medicines is higher than for other forms of medicine. It advised healthcare organisations to risk-assess injectable medicine procedures and products in all clinical areas, and develop an action plan to minimise high risks.

In 2008, the Patient Safety First campaign was launched, sponsored by the NPSA, the NHS Institute for Innovation and Improvement and The Health Foundation.³ One of the campaign's five key interventions is to reduce harm from unintended errors in the prescription, administration and reconciliation of high risk medicines.

Also in 2008, a report from the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) was published.⁴ This report investigated patients who died within 30 days of receiving systemic anti-cancer therapy, and raised serious concerns about the safe use of these medicines, in particular cytotoxic chemotherapy. Room for improvement in both clinical and organisational care was identified in 49% of trusts surveyed.

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Rituximab

Rituximab is a biological, systemic anti-cancer therapy, produced using recombinant DNA technology. It is licensed for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukaemia and rheumatoid arthritis.⁶

Rituximab targets CD20-positive B cell lymphomas, which account for 99% of all B cell lymphomas.⁷ It has been shown to be highly effective in the treatment of these haematological cancers, especially in combination with traditional chemotherapy drugs, and is recommended by the National Institute for Health and Clinical Excellence for a variety of lymphoma types.^{8,9} Its targeted approach to disease modification avoids many of the systemic side effects exerted by traditional chemotherapy drugs.

Rituximab is classified by the National Patient Safety Agency as a moderate risk product.² It has four risk factors:

- Therapeutic risk (as with all biological products)
- Complex dose calculation
- The requirement for part or multiple vials to be added to the infusion bag according to the dose requirement
- Use of a pump or syringe driver, for which the settings must be adjusted during the course of administration

At Northumbria Healthcare NHS Foundation Trust we decided that a proactive approach to the management of risks associated with rituximab was required. We decided to use the failure modes effects analysis (FMEA) tool.

FMEA

FMEA is a risk analysis tool that can be used to identify the points at which any process is likely to fail; to determine how potential changes might affect the safety of the process; and to monitor the impact of changes to risk over time.

It was originally developed as an engineering tool and was used in aerospace development in the 1940s–60s and in the motor industry in the 1970s–80s. It is now beginning to be adopted in healthcare. For example, the Scottish Patient Safety Programme recommends using FMEA to identify high risk areas as part of a reliable medicines management process.¹⁰

One of the advantages of using FMEA in healthcare is that it provides prospective risk analysis, which encourages the users of a process to map the stages within that process.¹¹ The users then identify where errors may occur (the failure modes) and score these modes based on the likelihood

of the error happening, the likelihood of detection of the error and the severity of the error if it was not prevented. These three scores are then multiplied to produce a final ‘risk priority number’ (RPN).

Method

The first step in the FMEA evaluation of rituximab was to observe and map the different stages of the rituximab process. Focus groups were then set up with the staff involved in the use of rituximab to identify the failure modes within each process stage. A pharmacist acted as project lead, facilitating the focus groups.

For each failure mode identified, the causes and effects associated with it were also identified. The failure modes were then given a score of one to 10 for their likelihood of occurrence, likelihood of detection and severity of effect on the patient, and these scores were multiplied to produce an RPN for each mode. Participants were advised to assign scores based on the ‘worst case scenario’. An example of the mapping and scoring process is shown in Figure 1 (p331).

Failure modes for which outcomes did not affect the patient (e.g. affects on paperwork for staff) were not included.

Failure modes with the highest RPN were analysed and their causes were discussed. Staff members involved in the processes then began to investigate any modifications that could lower the risk, repeating the FMEA process where appropriate to see if the overall risk had been reduced.

Results and discussion

The process stages identified for FMEA assessment were:

- Prescribing
- Pharmacy verification of prescriptions
- Aseptic production of the infusion
- Administration and monitoring

Prescribing The FMEA for the prescribing of rituximab was conducted by a specialist haematology nurse practitioner and consultant haematologist. From the RPNs calculated for this process, the two highest scoring failure modes were:

1. **Failure mode:** Failure to check the allergy status of the patient before prescribing rituximab
Cause: Failure to document a previous adverse reaction
RPN: 500

Because of the biological nature of rituximab, one of the most significant side effects is anaphylactic reactions caused by the body’s immune system recognising the drug structure as an antigen. In severe cases this can lead to cytokine release syndrome, which can be life-threatening.⁷

In this case, the high risk comes from the fact that if previous reactions are not documented, hypersensitivity cannot be predicted before prescribing the drug.

2. **Failure mode:** Incorrect records of a patient’s height and weight before dose calculation
Cause: Incorrect transcription of height and weight from previous prescription
RPN: 210

The incidence of incorrect transcribing of patients’ weight and height was deemed to be fairly high by those involved in the FMEA process, highlighting poor documentation. Patients are not weighed before each prescription is written, so alterations in weight between administrations are unlikely to be picked up. Under-dosing was deemed to be a considerable risk to the patient.

Pharmacy verification of prescriptions At the Trust, all prescriptions for systemic anti-cancer therapies are verified by a pharmacist trained in oncology before they are prepared and administered.

Two pharmacists and a technician were involved in the validation of the process map and FMEA for prescription verification and processing. The two highest scoring failure modes were:

At a glance...

What is FMEA? Failure modes effects analysis (FMEA) is a prospective tool that quantifies risks involved in different stages of a process. A scoring method is used to identify points of greatest risk and thus prioritise the areas requiring increased attention.

How can it be used? FMEA is being used increasingly in healthcare. At Northumbria Healthcare NHS Trust a pilot project was undertaken using FMEA to identify the risks associated with use of rituximab, and thus highlight areas for improvement.

What were the findings? The stages of the rituximab process found to have the highest risk were those associated with ineffective use of documentation. The causes of these effects were analysed by the staff involved in the process and steps were taken to reduce the risks. Several findings were applicable to other drugs of the same class.

Conclusion FMEA can be a useful tool in medicines management to assess and improve the safety of processes involving high risk drugs.

Point in the prescribing stage	Failure mode	Failure causes	Failure effects	Likelihood of occurrence (1-10)	Likelihood of detection (1-10)	Severity (1-10)	Risk priority number (RPN)
Dose calculation	Incorrect measurement of weight and height	Human error	Wrong dose given to patient	3	3	5	45
		Poor scale calibration		1	5		25
		Footwear not removed prior to measurement		1	1		5
		Incorrect units quoted or incorrect conversion		1	1		5
		Patient too ill to be measured		3	1		15
		Measurements transcribed incorrectly		7	6		210
	Incorrect calculation of body surface area	Human error	Wrong dose given to patient	3	2	5	30
	Incorrect dose or dosing frequency prescribed	Human error	Incorrect dose or dose frequency given to patient	2	1	5	10
		Wrong prescription form selected		2	1		10
		Calculator unavailable		2	1		10
Allergy status check	Allergy status of the patient not checked	Previous reaction not documented	Rituximab administered to patient with an allergy to rituximab/similar drug	5	10	10	500
		Previous reaction not identified	1	1	10		
		No notes available	3	1	30		

Figure 1: Example of the FMEA mapping and scoring method for the prescribing stage of the rituximab process (tables of the scores for the verification and administration stages are available on request from the authors).

1. Failure mode: Prescriptions received by the pharmacy department immediately before scheduled chemotherapy administration time
Cause: Incorrect schedule information from nursing staff
RPN: 360

For prescriptions received by the pharmacy less than 24 hours before administration was due, it was perceived that a higher incidence of incorrect schedules were received, and there would be less opportunity for thorough verification of prescriptions by the pharmacy team because they would not have time to check the patients' notes. This led to a higher RPN. However, since the consequence of this failure mode was re-prioritisation of the pharmacy workload, which has no direct affect on patients, this mode was discounted as a high risk problem.

2. Failure mode: Wrong body surface area calculated
Cause: Incorrect figures for height and weight stated on the prescription
RPN: 600

This was the highest scoring failure mode of all stages in the process and was compounded by the lack of ability of the pharmacy team to detect incorrect weights. This was given a high RPN since it could lead to incorrect dosing of rituximab.

Aseptic production of the infusion

After careful observation and process mapping of the aseptic preparation of rituximab, it was believed that the risks within this process were minimal. Each step had carefully documented standard operating procedures, was carried out by highly trained staff and double-checked at several points within the process. No high risk steps were identified.

Administration and monitoring

At the Trust, administration of rituximab takes place exclusively within the oncology day unit, where specialist haematology and oncology nurses are familiar with the administration of monoclonal antibodies.

The FMEA of administration and monitoring was performed by a specialist haematology nurse and staff nurse from the oncology day unit. This seems to be the

process stage associated with the most risks — six separate risks were identified, with scores ranging from 200 to 280. The three highest scoring failure modes were:

- 1. Failure mode:** Failure to identify an adverse reaction during observation of a patient during administration
Causes: Staff shortages or patients not reporting the symptoms of an adverse reaction
RPN: 280/200
- 2. Failure mode:** Patient not observed during administration of rituximab
Cause: High staff workload
RPN: 252

Clinical trials have shown that 50% of patients treated with rituximab experience symptoms that are indicative of an infusion-related reaction (ranging from fever, rigors or chills to nausea, headache, fatigue and tachycardia). More severe reactions such as cytokine release syndrome were found to affect about 10% of patients.¹ Infusion-related reactions are thought to occur one to two hours after the start of the infusion but

can be seen from 30 minutes to three hours afterwards, so appropriate monitoring is essential.

3. Failure mode: Incorrect completion of the administration schedule for rituximab

Cause: Reading the schedule incorrectly, incorrect transcription of the schedule or selection of the incorrect patient schedule from the electronic system.

RPN: 256

The rate of infusion of rituximab is recommended to be 50mg/hr at initiation, increasing in increments of 50mg/hr every 30 minutes, to a maximum of 400mg/hr. Alongside the pre-formatted prescription for rituximab, there is an administration table that prompts nursing staff to take observations of patients and increase the infusion rate as appropriate. This was designed as a safety step, but in this case was found to increase the risks if used incorrectly.

Lessons learnt

The use of rituximab at Northumbria Healthcare NHS Trust is considered to be a safe process. However, FMEA methodology has highlighted areas for improvement.

It has now been shown that some safety measures already employed do not fully eliminate risk and, as in the case of standardised administration schedules, can actually increase risks if not used appropriately.

Work is ongoing to modify the areas highlighted as being high risk. This includes:

- Redesign of prescription forms to include an allergy check box
- Inclusion of an allergy check in all pharmaceutical care plans
- Routine weighing of patients before prescriptions are written (this particular intervention has caused much debate and there are some practical challenges to overcome before it is adopted throughout the Trust).

It should be noted that several of the risk reduction strategies identified for rituximab are applicable to other systemic anti-cancer therapies, and to other high risk drugs.

A benefit of using FMEA is that rather than simply analysing procedures and documentation, the actual use of these procedures and documents by the healthcare

staff involved in the process is evaluated, to determine whether the safety tools have had their intended impact.

FMEA was also successful in engaging healthcare professionals in the risk assessment process. Instead of auditing the failures of the systems and feeding back the results, healthcare professionals personally involved in the processes were asked to identify weaknesses in their own systems. This approach seemed to be well received.

Furthermore, prospective risk analysis is not associated with the liability issues that surround the use of root cause analysis following an incident.

One of the successes of this project was the engagement with the wider clinical team. One of the consultant haematologists involved in the project commented: "This was the best use of time I have ever spent on patient safety."

A weakness of the FMEA method is that the scoring is subjective to those involved in the process, which makes the RPNs incomparable to those generated from other teams for other processes. However, where processes are similar, trends of the highest scoring failure modes can be compared.

Further work

Work is ongoing to modify the areas of rituximab use identified to have the highest risk. We plan to repeat the FMEA process for the use of rituximab in rheumatology, and for drugs within the same class for which there is less pharmacy involvement (e.g. infliximab).

Conclusion

FMEA was found to be an effective tool for identifying potential areas of risk in the use of rituximab, and the methodology could be applied to other high risk medicines.

Investigating the use of procedures and documentation by healthcare professionals who are actually involved in practice has the advantage of encouraging a reflective process to identify process flaws that may not have been identified using other risk assessment techniques.

Making changes to reduce harm from high-risk medicines is an area in which pharmacists are increasingly taking the lead. Pharmacists working with anti-cancer medicines should view this as part of a wider approach to reduce risk with all high risk medicines. We must be open to sharing good practice and be willing to learn from each other and from other non-medical professions.

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