King's College Hospital NHS
NHS Foundation Trust

Risk assessment for the reconstitution of monoclonal antibodies (mAbs) and procedure for the safe handling and administration of mAbs

Main Document Information	
Version:	1
Publication Date:	22/07/2024
Approval Body:	SACT Governance and lead chemotherapy consultant
Approval Date:	22/02/2024
Ratification Body:	Drugs and Therapeutics Committee
Ratification Date:	19/07/2024
Document Author:	**Laura Stevenson**
Review Date:	**22/07/2026**
Policy Category:	Clinical and Trust-Wide
Document Change from Previous:	New document
Readership (Target Audience):	Medical and Nursing staff
Relevant External Requirements:	To be used as national guidance

Document Location and History	
Current Document Title:	Risk assessment for the reconstitution of monoclonal antibodies (mAbs) and procedure for the safe handling and administration of mAbs
Current Document Location:	http://kingsdoc/docs/policies
Current Document Replaces:	
Previous Document Name:	N/A
Previous Version Number:	N/A
Previous Publication Date:	N/A
Location of Archived Document (delete as appropriate)**:**	http://kingsdoc/docs/policies or x:\Trust Wide Policies \ Archive – All out of date or superseded Trust Wide Policies

Document Authors	
Document Owner:	Laura Stevenson
Other Contributing Authors:	Chemotherapy Nurse Consultant and SACT governance members

Consultation Distribution		
Sent To		**Date**
Group:	SACT Governance	18/01/2024
	Drugs and Therapeutics Committee	19/03/2024
Team / Department:		
Individual:		

Version Control History				
Version	**Date**	**Type of Change**	**Summary of Changes**	**Author**
1	22/07/2024	New document	N/A	Laura Stevenson

Dissemination Schedule (Following Ratification)				
Target Audience	**Method of Distribution**	**Person Responsible**	**Confirmation Receipt Required?**	**Method of Replacement for Previous Version**
Nurses handling mAbs	KingsWeb		No	New document

Document Keywords	
Keywords:	Monoclonal antibodies, handling, risk assessment, exposure, patients, staff, Controlled system transfer devices.

Supporting Documentation (complete and added as appendices)	
Policy Checklist (delete as appropriate):	No
Equality Impact Assessment (delete as appropriate):	No
Ratification Sheet* (delete as appropriate):	No

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Contents

Summary
This risk assessment is intended to safeguard patients and staff, by defining acceptable standards of practice for the preparation and administration of monoclonal antibodies (mAbs) at Kings College Hospital NHS Foundation Trust.

N.B. Jump to appendix 1 for the risk assessment and associated documentation.

Introduction
Monoclonal antibodies (mAbs) were introduced into clinical practice in the mid-1980s, with their use in the healthcare setting increasing over the past decade. Their use has become established in the treatment of a variety of disease states including cancer, rheumatoid arthritis, transplant organ rejection, psoriasis and asthma.
Manufacturers have minimal data on the possible long-term risks of handling mAbs mainly because they are not required to provide this information for licensing purposes.
With the occupational risks in the handling of cytotoxic agents well-established, appropriate guidelines for their workplace handling have been developed.[1,10] However; there are no similar guidelines on the safe handling of mAbs in the clinical setting. Many current cytotoxic safe handling guidelines do not assess or provide guidance on how mAbs should be handled, particularly during their preparation and administration.

Pan London Guidelines (for Safe Prescribing, Handling and Administration of Systemic Anti-Cancer Therapy) advise that the preparation of mAbs should be individually risk assessed, taking into account the allergic potential based on the origin of the mAb and toxicities arising from the therapeutic use. An overall risk score should then be used to decide whether manipulation should be within an aseptic unit (high risk) or permitted in a clinical area (low/negligible risk).

All new mAbs must be risk assessed before being used within the Trust and this will be included in the submission to the New Drug Panel. For clinical trials, the risk assessment will be completed as part of the trial set-up process. Individual Trust approval via the Drug and Therapeutics Committee should be obtained for mAbs assessed as high risk being manipulated in clinical areas.

Type of risk
Guidance on the safe handling of monoclonal antibody products, published in 2015, by relevant NHS committees advises that risks associated with individual mAbs being handled requires an assessment of the nature of the product being handled based on both COSHH and pharmacological data, combined with knowledge of potential risks of exposure via internal exposure risks and toxicity, both presented below[11].
The outcomes of the handling and preparation risk assessments should be combined to create an overall risk assessment profile for the mAb concerned (High, Medium, Low risk)[11].
(Refer to Appendix 1 for Kings information regarding the scoring system for risk likelihood and risk impact.)
Literature suggests that mAbs have a different level of risk, in that their mode of action does not directly damage the genetic material, and therefore would not be expected to be carcinogenic, mutagenic or teratogenic in patients or healthcare staff preparing and handling these drugs[4,9].

Handling risk assessment: Internal Exposure Risk
Dermal exposure
The skin is an effective barrier to absorption of high molecular weight proteins. The upper limit for dermal absorption of compounds is around 500 Daltons to allow penetration of the stratum corneum.[5] Given that

mAbs have a much higher molecular weight (usually greater than 140kDa) the potential for dermal uptake of intact skin of unconjugated mAbs or intactconjugates in the occupational setting is unlikely.[4] As mAbs are immunoglobulin based they would also have restricted access across diffusional barriers unless transport is facilitated by specific mechanisms[8]. However, skin conditions such as dermatitis and other damage to the skin may facilitate the dermal uptake of monoclonal antibodies.[4]

Inhalation exposure

Exposure through inhalation during preparation of mAbs is possible though the risk is very low. A mouse-model study has shown that airway barriers are permeable to mAbs but passage into blood stream is limited, with estimates of bioavailability at 5% through inhalation[4]. However, given the high molecular weights of mAbs, the absorption rates could be considered lower. In areas where mAbs may be administered to patients via inhalation, the potential for exposure to the worker may be increased.[7]

Oral exposure

Monoclonal antibodies are intricately folded proteins that are easily susceptible to denaturation from environmental conditions.[8]If ingested through hand-to-mouth transmission, mAbs are rapidly broken down by gut enzymes and acids resulting in denaturing of the protein and loss of biological activity. Exposure via this route would be minimal.[4] However, there may be a theoretical risk from resultant lower molecular weight agents from conjugates which may be absorbed systemically. In the absence of occupational health studies, occupational risks from mAbs have also been extrapolated from the side effects of therapeutic doses and recommendations published.[4,9.]

One publication prepared a risk assessment tool based on the antigenic properties and the toxic potential of mAbs[9]. The other evaluated the reproductive and developmental toxicity and effects on fertility of several mAbs[4].While the evidence was lacking, the authors concluded that all of the mAbs evaluated had the potential for some level of reproductive toxicity. Both reviews were based on the extrapolation of occupational related toxicity from data obtained in therapeutic situations. This information alone may be misleading. Potential exposure pathways as discussed above were either not considered or authors concluded that exposure via these pathways would be very minimal. Any data extrapolated in this setting should be critically analysed factoring in aspects of routes of potential exposure.

Toxicity of individual monoclonal antibodies

Each individual monoclonal antibody should be risk assessed and assigned a Health and Safety Score. The risks from the Health and Safety Score and the NPSA assessment should be combined to establish the overall risk for each individual mAb (see below Appendix 2 for examples to follow). This overall risk will then be used to inform a decision for compounding the mAb within pharmacy facilities (for products with a high to moderate risk) or, due to capacity and other constraints permit preparation in a clinical area (low or low to moderate risk products).

A health and safety risk assessment should examine the allergic potential based on the origin of the mAb and various potential toxicities arising from the therapeutic use of the monoclonal antibody.

NPSA Risk assessment tool

The National Patient Safety Agency (NPSA) developed a risk assessment tool for injectable medicines after reviewing a variety of risk matrices currently in use in NHS organisations. The aim was to develop a risk

assessment matrix that could be recommended for use across the NHS. This tool helps to identify a product which has risks associated with it due to:

- Use of a concentrate
- Complex calculation or method
- Reconstitution of a vial
- Use of a part vial or more than one vial
- Use of an infusion pump driver

This tool is useful when assessing risks associated with the reconstitution of monoclonal antibodies and it will be used within the strategy for risk assessment of monoclonal antibodies.

In particular, an NHS organisation should use this guidance only within the framework of its strategic risk appetite and risk management decision-making process.

Health and Safety Risk Rating

The health and safety assessment examines the allergic potential based on the origin of the mAb. A numerical score from 1 to 3 is assigned according to the content of foreign protein in the product; 3 for murine, 2 for chimeric and 1 for fully humanised.

In addition, toxicities arising from the therapeutic use of mAbs should be assessed using toxicity warnings from the summary of product characteristics datasheets, published toxicity warnings and health and safety datasheets, where available.

Overall risk assessment

The scores from the NPSA risk assessment and health and safety risk rating are then added together to give a risk rating as below:

1 to 3 = low risk
4 to 5 = moderate risk
6 and above = high risk

See Appendix 1 for more details on how to carry out the risk assessment.

Risk definitions

The overall risk could then be used to inform a decision for compounding the mAb within pharmacy facilities (for products with a high to moderate risk) or, in the event of capacity and other constraints, permit preparation in a clinical area (low or low moderate risk products).

- **High risk**
  If both handling and preparation risk assessments are high or the handling risk assessment alone is high. For these products only preparation in a pharmacy aseptic unit is possible.
- **Moderate risk**
  If the handling risk assessment is medium or the preparation risk assessment medium or high. Suitable risk mitigation controls must be put in place. (see below)
- **Low risk**

If both handling and preparation risk assessments are low. Product may be prepared in clinical areas with no further controls required apart from standard ward based aseptic technique.

Risk Mitigation Strategies for Moderate Risk mAbs

Personal Protective Equipment (PPE)

PPE materials are usually readily available in the hospital and an easy and safe measure to implement. PPE has the ability to protect staff working with mAbs but would not fully eliminate mAbs from the air and could affect other staff in the vicinity who are not wearing PPE.

Appropriate personal protective equipment (PPE) (which occupies the fourth place in the hierarchy of protection measures of the ISOPP standards) includes protective gloves, gowns, facial protection and mob caps/hairnets; should be made available to all healthcare workers who may come in contact with high risk products. Moreover, it is critical that healthcare workers be educated in the appropriate selection and use of PPE for protection against exposure to these monoclonal antibodies.

Closed system devices

Closed-system drug transfer devices (CSTDs) are devices which mechanically prohibit the transfer of environmental contaminants into a system as well as the escape of hazardous drug or vapour concentrations outside the system. They have been specifically designed to protect healthcare workers from occupational exposure to hazardous substances.

The devices themselves are expensive, as they are one use only. Training of staff on the appropriate use of CSTDs would be required to implement the process. UKONS and the UK SACT board both have both released statements on the effectiveness on CSTDs[14]; and cochrane have undertaken a systematic review based on their findings into CSTDs.[14] They concluded that there is currently no evidence of differences in exposure or financial benefits between CSTDs plus safe handling versus safe handling alone (very low quality evidence). They also found an absence of reporting of health benefits by any of the studies they reviewed, the systematic review authors concluded that there is currently no evidence to support or refute the routine use of closed-system drug transfer devices in addition to safe handling of infusional hazardous drugs.

Use of CSTDs is controversial and an inefficient use of resource, with a systematic review demonstrating no evidence of differences in exposure between safe handling plus CSTD vs safe handling alone. The lack of evidence and absence of reporting of health outcomes places the financial burden under question and renders it unviable currently.[14]

The systematic review authors also disagreed with any guidelines or recommendations that CSTDs should be used routinely whenever possible.

Outsourcing

Some monoclonal antibodies are outsourced by pharmacy aseptic services, such as Rituximab. These monoclonals have extended stability studies and therefore longer expiry dates; these types of monoclonals are also usually dose banded making it easier to order products in as stock, meaning the dose is readily available as an off the shelf product.

Monoclonal antibodies with short expiries cannot be outsourced and must be made in the trust either at ward level or in aseptic services. All monoclonal drugs that have a cytotoxic component i.e. Trastuzumab

emtansine (Kadcyla®) must be made in a manufacturing unit, either in the hospital or in licensed outsourcing facility.

Reconstitution in the aseptic unit

It is not feasible for all mAbs to be prepared in the Aseptic unit due to capacity constraints.

When mAbs are prepared at ward level, staff should use aseptic non-touch technique to prepare the doses. Proper technique will mitigate handling and exposure risks to ward personnel.

Implementation of new monoclonal antibodies

All new monoclonal antibodies must be risk assessed by an appropriately trained pharmacist before being used within the Trust.

All relevant data sheets and documentation (e.g. COSHH data sheets, Investigators brochure, SPCs, MEDUSA guidance) will be reviewed and then the NPSA risk guidance assessment tool will be utilised alongside the King's mAb risk assessment form. The product will then be assigned a risk level and thereafter an appropriate area and method for reconstitution will be decided.

The assessor will then complete the risk assessment using the mAb risk assessment form (appendix 1) as well as the 'Medication Risk Assessment form' required for all new medicines. These will determine if the product is suitable for preparation in a clinical area or if it must be prepared in the Pharmacy Aseptic Unit.

The completed mAb assessment must then be approved and signed by:

- The Chemotherapy Nurse Consultant or the Matron for CDU for haematology areas
- Specialist nurse or matron for other specialist ward areas
- The Consultant or Specialist/Principal Pharmacist for the specialty, or the Associate Chief/Principal/Specialist Pharmacist Aseptic Services.
- The New drug panel

If the product is approved for preparation in the clinical area then the generic procedure for preparation of monoclonal antibodies in clinical areas and the protocol for the relevant regimen, if relevant, should be followed.

Generic procedure for preparation of monoclonal antibodies in clinical areas

- Wash hands according to King's Hand Hygiene policy (WHO guidelines on hand hygiene)
- Don appropriate personal protective equipment at all times:
    - **Mandatory** - A pair of sterile nitrile gloves (apron and face mask optional)
- Ensure the working surface is clear of clutter and ensure it is clean before commencing preparation.
- Prepare the dose using a plastic tray following the product-specific MEDUSA guidance, and using Aseptic Non-Touch Technique (ANTT) to ensure best practice as poor technique maybe instrumental in causing a Healthcare Acquired Infection. ANTT should consist of:
    - Effective hand washing
    - Wearing appropriate protective clothing where required

- Identifying key parts and key sites
- Avoiding touching those key parts during the procedure

- In general, intravenous lines will be primed with diluent unless otherwise specified in the protocol or prescription

- Discard any sharps and empty vials in a sharps bin and any other waste in a clinical waste bin. Empty vials that need to be returned to pharmacy (e.g. for clinical trials) should be wiped clean with Clinell/alcohol wipes and sealed in the plastic re-sealable bag that they were supplied in.

- The final prepared product and the plastic tray must also be wiped clean to remove any residues on the outer surface. Used wipes must be discarded in a clinical waste bin.

- Wipe down the work surface again using Clinell/alcohol wipes and discard gloves, face mask and apron (if worn in a clinical waste bin.

- Gloves and aprons worn during administration should be removed immediately after use, disposed of appropriately and not worn outside of the clinical area.

- After use the tray used to contain the product must be cleaned using Clinell/alcohol wipes. Used wipes must be discarded in a clinical waste bin. If there has been any spillage into the tray then the tray must be washed thoroughly with water and detergent.

- If more than one injectable medicines needs to be prepared then it must be prepared and administered before another one is made i.e. no batch production should take place. Preparing multiple doses at one time could lead to errors and patient harm.

- Second check of the final product from a member of staff accredited to do so.

For completed/administered mAbs:

- Wear appropriate PPE
- Do not disconnect the giving set from the infusion bag
- Double wrap the drip tubing and empty infusion bag and place in a waste container
- Sharps should be put directly into a waste container and not left lying on any surface before disposal
- Avoid the risk of aerosol formation contaminated sharps, giving sets and tubing should be disposed of intact and not clipped or cut;
- Used disposable equipment: gloves and any other items that have been in contact with mAbs should be put into a waste container

Spillage and disposal

Refer to Standard operating procedure: Cleaning Cytotoxic Spillages Emergency Procedure which should be available on the unit where mAbs are prepared. All healthcare professionals involved in the reconstitution of monoclonal antibodies should be aware of and familiar with this procedure. Cytotoxic spill kits should always

be available in all clinical areas where mAb reconstitution is taking place. If the infusion bag carrying the mAb has been punctured and there is significant leakage, it is recommended that healthcare staff deal with this as a spillage as outlined in instructions in the cytotoxic spill kit.

Training

Pharmacists and pharmacy technicians

Pharmacy staff involved in the screening, preparation or reconstitution of monoclonal antibodies must be familiar with this protocol and pharmacists who will be undertaking risk assessments for individual monoclonal antibodies will require specific training by the Principal Pharmacist – Haematology and Oncology or the Principal Pharmacist – Aseptic Services.

Nursing staff and other healthcare professionals

All nursing and other staff involved in the preparation or administration of monoclonal antibodies must have read and understood the trust policy on administration of Intravenous drugs and other policies referred to throughout. For monoclonal antibodies used within the oncology or haematology setting the administering nurse must be signed off appropriately for administration. For monoclonal antibodies used in any other setting nurses must have completed the relevant training for intravenous drug administration, and be signed off by the PDN or Nurse specialist.

As with all drugs to be reconstituted at ward level all new mAbs should be assessed for education and training needs appropriate for the specific setting, as part of the overall risk reduction strategy. Education and training can be formal or informal, self-directed or in-house.

Systems must be in place for the reporting incidents involving accidental spillage and potential exposure to mAbs. All clinical incidents such as adverse events and near misses involving must be documented, reviewed and learning shared to minimize future errors.

References

1. Preventing occupation exposure to cytotoxic and other hazardous drugs, European Policy Recommendations
2. National Institute for Occupational Safety and Health (NIOSH). 2004 “NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings”. Available at: http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf.
3. Centers for Disease Control and Prevention (CDC). 2004. “Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings”. Available at: http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf.
4. Halsen G, Kramer I. Assessing the risk to health care staff from long-term exposure to anticancer drugs – the case of monoclonal antibodies. J Oncol Pharm Pract 2011; 17:68-80
5. Bos J, Meinardi M. The 500 dalton rule for the skin penetration of chemical compounds and drugs. Exp Dermatol 2000; 9:165-9
6. Maillet A, Guilleminault L, Lemarie E, et al. The airways, a novel route for delivering monoclonal antibodies to treat lung tumors. Pharm Res 2011; 28:2147-56
7. Maillet A, Congy-Jolivet N, Le Guellec S, et al. Aerodynamical, immunological and pharmacological properties of the anticancer antibody cetuximab following nebulisation. Pharm Res 2008; 25:1318-26
8. Vermeer A, Norde W. The thermal stability of immunoglobulin: unfolding and aggregation of a multi-domain protein. Biophys J 2000; 78:394-404
9. Langford S, Fradgley S, Evans M, Blanks C. Assessing the risk of handling monoclonal antibodies. Hosp Pharm 2008; 15:60-4
10. EASTY, A.C. et al. Safe handling of cytotoxics: guideline recommendations. **Current Oncology**, [S.l.], v. 22, n. 1, p. e27-e37, sep. 2014. ISSN 1718-7729. Available at: <https://currentoncology.com/index.php/oncology/article/view/2151/1710>. Date accessed: 02 aug. 2019. doi:http://dx.doi.org/10.3747/co.22.2151.
11. Guidance on the safe handling of monoclonal antibody (mAb) products, November 2015, NHS Pharmaceutical Quality Assurance Committee 2015
12. National Patient Safety Agency Alert 20, March 2007
13. De Lemos M, Badry N et al. Safe handling of monoclonal antibodies: Too large to be hazardous? J Oncol Pharm Pract 2017; Volume: 24 issue: 3, page(s): 218-220.
14. Gurusamy KS, Best LMJ, Tanguay C, Lennan E, Korva M, Bussières JF. Closed-system drug-transfer devices plus safe handling of hazardous drugs versus safe handling alone for reducing exposure to infusional hazardous drugs in healthcare staff. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD012860. DOI: 10.1002/14651858.CD012860.pub2.

Appendix 1

mAb risk assessment for Operator Handling

Part 1 Health and Safety score		
Origin (O)	≥ 75% humanised (suffix – zumab or mumab)	**1**
	Partially humanised (chimeric; suffix –ximab)	**2**
	Bispecific antibodies (binds to 2 different anitgens - BsAbs)	**2**
	Completely murine (mouse or hamster protein; suffix –momab)	**3**
Toxicities arising from therapeutic use (T)	Low risk of harm to the operator	**1**
	Theoretical risk of immunological, cutaneous or haematological adverse effects to the operator with prolonged low-dose exposure	**2**
	Known risk of immunological, cutaneous, haematological or other adverse effects to the operator with prolonged low-dose exposure	**3**
	Known or potential teratogenic or embryotoxic properties	**4**
	Known cytotoxic, radioactive or risk of initiating a cancer	**5**
Health & Safety score (O+T)	**1-3 = low risk** **4-5 = moderate** **6+ = high**	

NPSA risk assessment for preparation and administration

Part 2 NPSA 20 risk assessment		
Risk factors	**Description**	✓
Therapeutic risk	Where there is a significant risk of patient harm if the injectable medicine is not used as intended.	
Use of a concentrate	Where further dilution (after reconstitution) is required before use, i.e. slow iv bolus not appropriate.	
Complex calculation	Any calculation with more than one step required for preparation and/or administration, e.g. microgram/kg/hour, dose unit conversion such as mg to mmol or % to mg.	
Complex method	More than five non-touch manipulations involved or others including syringe-to-syringe transfer, preparation of a burette, use of a filter.	
Reconstitution of powder in a vial	Where a dry powder has to be reconstituted with a liquid.	
Use of a part vial or ampoule, or use of more than one vial or ampoule	Examples: 5ml required from a 10ml vial or four x 5ml ampoules required for a single dose.	
Use of a pump or syringe driver	All pumps and syringe drivers require some element of calculation and therefore have potential for error and should be included in the risk factors. However, it is important to note that this potential risk is considered less significant than the risks associated with not using a pump when indicated.	
Use of non-standard giving set/device required	Examples: light protected, low adsorption, in-line filter or air inlet.	
Total number of product risk factors	✓ = **1** **Score** 6+ = **high-risk product (Red).** 3 - 5 = **moderate-risk product (Amber).** 1 - 2 = **lower-risk product (Green).**	

Overall risk assessment score

Health & Safety Score (Part 1)	NPSA Score (Part 2)	Preparation details
Low	Green	Ward level
Low	Amber	Ward level
Low	Red	Ward level
Moderate	Green	Ward level
Moderate	Amber	Aseptics or ward level depending on review by pharmacy team*
Moderate	Red	Aseptics
High	Green	Aseptics
High	Amber	Aseptics
High	Red	Aseptics

*Review will consist of manufacturer or COSHH information based on product handling, if any handling concerns are identified the products will be prepared in Aseptic Services.

This product has been assessed as ……risk and will therefore be prepared by ……

Risk assessment completed by: Date:

Agreed by Consultant Chemotherapy Nurse or specialist nurse and matron for the clinical area: Date:

Agreed by Senior Aseptic Pharmacist: Date:

Approved by (new drugs panel): Date:

Appendix 2

Examples

Health and Safety Risk Rating for monoclonal antibodies prepared at KCH

ATEZOLIZUMAB

Significant toxicity from SPCs or SDS:

Not hazardous

Origin of monoclonal:

Fully humanized, engineered monoclonal antibody

Immunogenicity:

Classification not possible - no information available

Carcinogenicity:

Classification not possible - no information available

Genotoxicity:

Monoclonal antibodies are not expected to alter DNA or chromosomes.

Teratogenicity:

Parenteral administration to pregnant women can cause foetal harm.

Risk rating: Moderate

DARATUMUMAB

Significant toxicity from SPCs or SDS:

Not hazardous

Origin of monoclonal

100% humanised monoclonal antibody produced in Chinese Hamster Ovaries

Immunogenicity:

Classification not possible - no information available

Carcinogenicity:

Systemic exposure from handling is expected to be negligible, therefore not carcinogenic

Genotoxicity:

Routine genotoxicity studies are not applicable as Daratumumab cannot diffuse into cells and interact with DNA or chromosomal material

Teratogenicity:

Embryo/foetal harm from worker exposure is considered unlikely.

Risk rating: score: Low

INOTUZUMAB

Significant toxicity from SPCs or SDS:

Inotuzumab is a cytotoxic drug and should be handled with care

Origin of monoclonal:

Inotuzumab ozogamicin is an antibody-drug conjugate (ADC) composed of a humanized IgG4 kappa monoclonal antibody (inotuzumab) linked to a small molecule cytotoxic agent (N-acetyl-gamma-calicheamicin dimethylhydrazide)

Immunogenicity:

The incidence of antidrug antibodies to inotuzumab is low and is not clinically meaningful

Carcinogenicity:

In animal studies, preneoplastic and neoplastic lesions occurred at lower exposures than exposures seen following human clinical exposure

Genotoxicity:

Inotuzumab ozogamicin was clastogenic in the bone marrow of male mice, inotuzumab is known to be mutagenic

Teratogenicity:

Based on non-clinical safety findings, inotuzumab ozogamicin can cause embryo-foetal harm when administered to a pregnant woman. Studies in animals have shown embryo-foetal toxicity. Male and female fertility may be compromised by treatment with inotuzumab.

Risk rating: High

Examples - NPSA Risk assessment tool

Drug Name	Prepared injectable medicine	Bag (B) / Syringe (S) / Infusor (I)	Therapeutic Risk	Use of concentrate	Complex calculation	Complex preparation	Reconstitute vial	Part/multiple container	Use of infusion pump/driver	Non standard infusion set	Total Risk Factors	Risk when prepared in a clinical area	Ready to use in UK
Atezolizumab	IV infusion	B	Y	Y	x	x	x	Y	Y	x	4	Amber	No
Daratumumab	SC injection or IV infusion	B	Y	Y	x	x	x	Y	Y	Y	5	Amber	No
Inotuzumab	IV infusion	B	Y	x	x	Y	Y	Y	Y	x	5	Amber	No

Examples - Overall risk rating for each monoclonal antibody and preparation details

The risks from both the health and safety assessment and the NPSA assessment are combined to establish the overall risk for each individual mAb.

Monoclonal Antibody	Health and safety risk rating	NPSA risk rating	Overall risk rating	Preparation details
Atezolizumab	Moderate	Amber	Moderate	**Aseptics**

Daratumumab	**Low**	**Amber**	**Low**	**Ward level**
Inotuzumab	**High**	**Amber**	**High**	**Aseptics**