



**Specialist
Pharmacy
Service**

Multiple Use of Injectable Medicines in Clinical Areas

**Produced in collaboration by QA,
Medicines Use and Safety and
Medicines Information**

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**The first stop
for professional
medicines advice**

Intended audience

This document is intended for multi-professional clinical practitioners to use as a reference and source of information for the prescribing, reconstituting or administering injectable medicines. Chief Pharmacists, Medicines Safety Officers (MSO) and other pharmacy staff involved in the governance of injectable medicine should ensure that local policies are in line with the guidance contained within this document.

Scope

This document provides guidance on the multiple use of injectable medicines (vials, ampoules, infusion bags) **in clinical areas**. The term *multiple use* includes use of a single container of an injectable medicine

- To administer more than one dose to a single patient and/or
- To administer one or more doses to more than one patient

The advice in this document is in addition to and supportive of principles outlined by NPSA 20 “Promoting the Safer Use of Injectable Medicines”¹ and further defined in 2017 by the QA Advice Note to Chief Pharmacists² i.e. any injectable prepared in a clinical area should be administered immediately (within 30 minutes) and administration should be complete in less than 24 hours.

Aseptic Preparation of Injectable medicines in Aseptic Dispensing Units or Radiopharmacy Units are *outside* of the scope of this document and should refer to the Yellow Cover Document “Vial Sharing in Aseptic Services 1st Edition August 2014”³.

Storage of medicines is also outside the scope of this document. The ‘Safe and Secure Handling of Medicines’⁴ should be referred to where this information is required.

Radiopharmaceuticals are outside the scope of this document. UKRG Advice on the safe drawing up of radiopharmaceuticals⁵ should be consulted.

Overview

Injectable medicines come in three main presentations:

- IV infusion bags
- Vials
- Ampoules

(Ready-to-Administer injectable medicines e.g. pre-filled syringe are also available)

Some injectable medicines contain preservatives which are added to permit the container to be used as a multi-dose container, prevent in-use contamination of the product, and reduce risk of a patient acquiring an infection when the preparation is administered³.

A Licensed Medicine is one where review of the safety, efficacy and quality of the product by the regulatory body results in approval of a Marketing Authorisation and assignment of a Product Licence (PL) number or EU number. A PL number is assigned by the UK's regulatory body, the MHRA. An EU number is assigned via the EMA. A licensed medicine in the UK is identifiable from the PL or EU number on the product and the PL or EU number in the Summary of Medicinal Product Characteristics (SmPC) or Patient Information Leaflet (PIL).

A Licensed Medicine must be used as directed in the Summary of Medicinal Product Characteristics (SmPC). If the product is used or prepared in a different way to that stated in the SmPC, the product becomes "off-label" and the liability for that use may transfer from manufacturer to the health care provider. This is particularly relevant to injectable medicines where most are licensed for single use only. Use of a single-use injectable medicine for multiple doses is therefore not in line with the SmPC, and therefore liability for that use transfers from the manufacturer to the healthcare provider.

Some injectable medicines do not have a UK product licence and practitioners should be aware of the licensed status when prescribing, reconstituting and administering these medicines (see local Unlicensed Medicine Policies). Appendix 1 shows the Royal Pharmaceutical Society hierarchy of risk in prescribing these medicines⁴.

As an unlicensed medicine results in a higher risk category, the organisation holding responsibility for the safety, quality and efficacy must be aware of and comfortable with the risks associated with its use and any steps taken to mitigate individual risks.

The majority of injectable medicines are unpreserved. As such microbiological risks require management. The large numbers of micro-organisms found in wards and clinical areas present a risk to injections in use, as contamination may be introduced when the ampoule is opened or the vial closure punctured. This risk is minimised by administration immediately after preparation. During subsequent storage, even of a few hours, micro-organisms can proliferate and present a risk of infection to the patient.

This risk is greatly increased if "coring" occurs – this is where the passage of a hypodermic needle through a vial closure removes a small piece of rubber, creating a patent opening between the outside environment and the sterile contents of the injection vial, through which contamination can pass. This risk can be managed in pharmacy aseptic preparation units by manipulating injections in a high grade environment, from which all micro-organisms are excluded but cannot be adequately controlled in clinical areas.

Complexity of preparation also increases microbiological risk. The greater the number of aseptic manipulations, the greater the risk of inadvertent contamination. This risk can be managed with careful aseptic non-touch technique, but cannot be removed.

Considerations for Local Injectable Use

IV INFUSION BAGS

IV Infusion bags are not routinely preserved and are licensed for **single patient - single use only**. This includes simple IV fluids which should not be used to reconstitute multiple doses. This is due to:

- **PATIENT RISK**

This is associated with increased microbiological risk due to cross contamination and multiple manipulations to prepare the product. This could potentially result in patient harm via bacteraemia.

- **RISK TO ORGANISATION**

Multiple use of an unpreserved bag is outside of the Marketing Authorisation thus responsibility lies with the organisation, not the manufacturer.

AMPOULES

Ampoules are not routinely preserved and are licensed for **single patient - single use only**. Only one withdrawal from any ampoule is considered compliant with the requirements of aseptic technique. Ampoules should be drawn up immediately after opening as once open, they are unprotected from environmental contamination which presents microbiological and particulate risks:

- **PATIENT RISK**

This is associated with increased microbiological risk due to cross contamination and multiple manipulations to prepare the product. This could potentially result in patient harm via bacteraemia.

- **RISK TO ORGANISATION**

Multiple withdrawals from any ampoule are outside of the Marketing Authorisation thus responsibility lies with the organisation not the manufacturer. The increased likelihood of patient harm also increases the risk of litigation claim.

VIALS

Two types of vials are used:

Unpreserved Vials

These are not preserved and are licensed for **single patient - single use only** and should not be used to reconstitute multiple doses. This is due to:

- **PATIENT RISK**

Associated with increased microbiological risk due to cross contamination and multiple manipulations to prepare the product

- **RISK TO ORGANISATION**

Multiple use of an unpreserved vial is outside of Marketing Authorisation thus responsibility lies with the organisation not the manufacturer.

Preserved Vials

As written in the terms of a Marketing Authorisation and as stated in a SmPC, these vials can be used for multiple doses. Organisations therefore need to establish in their policy whether there will be any consideration of multi-patient, multi-dose vials or if multi-dose vials are to be restricted to individual patients (e.g. Insulin).

It is recommended that organisational policies are clear on how multi-use vials are used within each organisation. This local policy decision should take into account that **even where intended for multiple use**, containers shared between patients, can act as a vector in the transmission of infection^{6,7}.

Injections for multiple-use contain antibacterial preservatives. These prevent the proliferation of any bacteria introduced during use, but are not effective against viruses, protozoa, or other organisms, such as those causing malaria^{8,9,10}.

For reasons of economy and convenience, the practice of “multi-dosing” from a container intended for single use has, on occasion, been seen in clinical situations. This practice is not recommended and should be eliminated as it presents a risk to medicines, and therefore to patients.

It is recommended the following factors must be considered **as a minimum** when considering using multi-dose vials for multi-patient use:

- Patient Factors (Such as age, condition, indication, immunocompromised etc.)
- Environmental (Such as Preparation area, storage, distraction, training, patient throughput, transferring product with patient etc.)
- Organisational (liability considerations, economic benefit vs risk assessment, etc.)

An example of the sort of assessment an organisation may perform for an individual medicine is given below.

| FACTORS CONSIDERED FOR SUITABILITY OF PRESERVED INJECTABLE MEDICINES FOR USE IN MULTIPLE PATIENTS | | | |
|---|---|--|---|
| MULTI-USE INJECTABLE MEDICINE | PATIENT RISK | ENVIRONMENTAL RISK | ORGANISATIONAL RISK |
| Insulin Brand X strength y units /ml | Diabetic patients, likely to be prone to infection and elderly. Risk of transmission of infection if used for multiple patients. Preservatives ineffective against viruses. | Administered by nursing staff on ward, simple draw up in prep room. No patient throughput. Fridge storage. | This medicine is inexpensive. No current issues with supply. Potential for liability if a patient becomes infected. |
| Risk Mitigation | Multi-use for single-patients only. | Risk mitigated via local procedures and training. | Muti-dose for one patient only. |
| Trust Position | Multi dose insulin can be used for individual patients only. This must be incorporated into local policies | | |

Figure 2: Sample Risk Assessment for using Multiple -Use Vials in Multiple-Patients using RAG rating to indicate risk

Where economic factors are involved, options for risk mitigation consideration include vial sharing in an aseptic unit.

Summary

It is recommended that unpreserved IV infusion bags, ampoules and single-use vials should only be used for one dose for one patient and then be discarded. In the instances where a preserved multi-dose vial is used, a risk assessment should be performed to determine if it is acceptable to use the multi-use vial for multiple patients. Local Policies should be implemented to correspond to the recommendations set out below.

| PRESENTATION | NUMBER OF PATIENTS - TYPE OF USE |
|------------------|--|
| IV BAG | SINGLE PATIENT - SINGLE USE ONLY |
| AMPOULE | SINGLE PATIENT - SINGLE USE ONLY |
| UNPRESERVED VIAL | SINGLE PATIENT - SINGLE USE ONLY |
| PRESERVED VIAL | SINGLE PATIENT – MULTIPLE USE or RISK ASSESSMENT |

Table 1: Summary of guidance on the multiple use of injectable medicines

References

1. NPSA. Patient Safety Alert 20 “Promoting the Safer Use of Injectable Medicines” 2007.
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https://www.cdc.gov/injectionsafety/ip07_standardprecaution.html
10. Al-Saigul AM, Fontaine RE, Haddad Q. Nosocomial malaria from contamination of a multidose heparin container with blood. Infect Control Hosp Epidemiol. 2000 May; 21(5):329-30.

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Appendix 1

| What the MHRA does: | Origin of the medicine: | What prescribers and pharmacists should consider: |
|---|---|---|
| <ul style="list-style-type: none"> ■ MHRA/EMA assesses and approves individual products and the manufacturer's premises and processes ■ Appropriate standards of quality, safety and efficacy are met | EU or UK licensed medicine | <ul style="list-style-type: none"> ■ Use of the medicine in accordance with its Marketing Authorisation |
| <ul style="list-style-type: none"> ■ MHRA assesses and approves individual products and the manufacturer's premises and processes ■ Appropriate standards of quality are met | Off-label (unlicensed) use of EU or UK licensed medicine | <ul style="list-style-type: none"> ■ Assessment of the safety and efficacy of off-label use ■ Risks of using the medicine outside the terms of the Marketing Authorisation |
| What the pharmacist is responsible for: | | |
| <ul style="list-style-type: none"> ■ MHRA evaluates and assesses import notifications for individual medicines (see also definitions) ■ The regulator in the country of origin assesses and approves individual products and the manufacturer's premises and processes: this may or may not be equivalent to the UK | Imported product licensed in country of origin** | <ul style="list-style-type: none"> ■ Assessing clinical suitability ■ Clinical suitability and licensed indications ■ Sourcing from a country with an equivalent regulatory framework to the UK ■ Checking that manufacturing standards are equivalent to EU GMP ■ Controlling risks of medication error because of unfamiliar/foreign language packaging, labelling and leaflets |
| <ul style="list-style-type: none"> ■ MHRA inspects and approves the MS Licence holder's premises and processes, but not individual products | UK Special manufactured by MS Licence holder | <ul style="list-style-type: none"> ■ Assessing clinical suitability ■ Checking manufacturer has an appropriate licence ■ Ensuring product meets the purchasing specification ■ Assess the evidence that supports the formulation and shelf life |
| <ul style="list-style-type: none"> ■ No MHRA oversight. The medicine is made under the supervision of a pharmacist in response to a prescription | Made under pharmacist supervision Extemporaneously prepared medicine | <ul style="list-style-type: none"> ■ Assessing clinical suitability ■ Ensuring the medicine is made in a registered pharmacy ■ Ensuring product meets the purchasing specification ■ Assess the evidence that supports the formulation and shelf life |
| <ul style="list-style-type: none"> ■ MHRA evaluates and assesses import notifications for individual medicines ■ There may be no regulatory framework in the country of origin | Imported medicine not licensed in country of origin | <ul style="list-style-type: none"> ■ Assessing clinical suitability ■ Checking that manufacturing standards are equivalent to EU GMP ■ Ensuring product meets the purchasing specification ■ Obtaining evidence that the formulation and shelf life are validated ■ Controlling risks of medication error because of unfamiliar/foreign language packaging, labelling and leaflets |

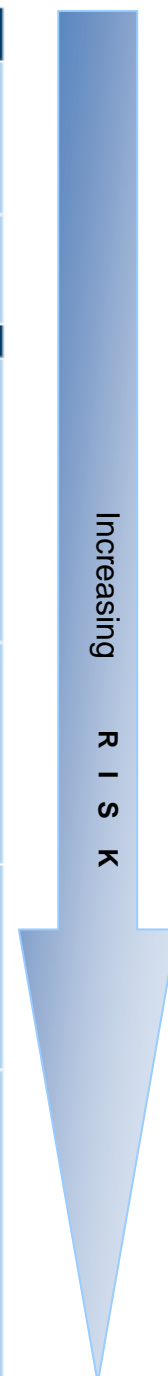


Figure 1: RPS GUIDE TO PRODUCT OPTIONS WHEN NOT SUPPLYING A LICENSED MEDICINE* (*See also MHRA guidance note 14; appendix 2. **Countries with an equivalent regulatory framework are European Economic Area countries, and countries with mutual recognition agreements. Medicines licensed in other countries may not be subject to safeguards equivalent to GMP.)