# NHMC

National Homecare Medicines Committee

# RPS Handbook for Homecare Services - Appendix 23:

# Maintaining "the Cold Chain" in patients' homes - Guidance for temperature control, storage & handling of homecare medicines by patients

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## 1 Introduction

Medicines will be stored and handled in patients' homes in accordance with the manufacturer's instructions to ensure their quality is not compromised. This will optimise safety and effectiveness of treatment in the homecare setting whilst minimising wastage. In the non-homecare supply chain, medicines which need refrigerated storage are expected to be handled at room temperature for dispensing and transport to patients' homes; this is accounted for when shelf lives are assigned by the manufacturer.

This guidance supplements information published in the RPS Handbook for Homecare Services[1] the aims to assist pharmacists in taking professional risk-based decisions when implementing homecare services for medicines requiring cold-chain storage.

It includes advice and signposts resources on:

- assessing individual medicines to determine their storage and monitoring requirements
- choosing appropriate refrigeration and monitoring equipment
- recognising, understanding and managing temperature excursions

It is recognised that some medicines have special characteristics which make them less suitable for community pharmacy and/or hospital outpatient supply due to the additional risk control measures that are available within homecare services needed to maintain patient safety. Within homecare services, it is possible to implement risk controls that are difficult to achieve via other supply routes. Risk control measures necessary to mitigate risks associated with those special characteristics must be fully documented and known to healthcare professionals delivering that homecare service. This should be taken into account when designing and implementing homecare services.

## 2 Scope

This document applies to medicines that have been supplied via homecare services which require storage between 2ºC – 8ºC in a patient's home and to the equipment required for their storage. However, the same principles may be applied to medicines requiring storage at other temperature ranges.

[1] https://www.rpharms.com/recognition/setting-professional-standards/homecare-services-professional-standards

This document does not apply to the storage of medicines in places other than a private home (e.g. residential or nursing home, or healthcare settings such as clinics and hospitals).

The assessment of the ability of patients to comply with the storage and monitoring requirements for their medicines is out of scope of this guidance, but will be considered when assessing the suitability of homecare services as a route of supply of medicines for individual patients.

## 3 Principles

- Safe storage of medicines supplied to the patient by community pharmacies, hospital outpatient pharmacies or via homecare medicines services is the responsibility of the patient.
- Storage controls and monitoring requirements will be kept as simple and easy to manage as possible, and proportionate to the risk of temperature deviations on patient safety and potential for medicine wastage.
- The amount of stock held by the patient will reflect the optimum balance between patient convenience, available storage space, and minimising the impact of any temperature excursions or other storage incidents.
- Storage conditions in the Summary of Product Characteristics apply to long term storage of medicines within the pharmaceutical supply chain. Rigid adherence during (relatively short term) storage in the patient's home may only be necessary for medicines where there are significant product stability issues as detailed in the Summary of Product Characteristics.
- A risk assessment will be used to determine the storage and temperature monitoring requirements for each homecare medicine and how best they may be met. Some residual risks may need to be accepted.
- Homecare medicines are often high-cost medicines. Wastage of medicines should always be minimised but may be justified if there is inadequate evidence of appropriate storage in cases where the risk to medicine quality and/or patient safety is judged as significant.

## 4 Risk assessment

Recommendations for home storage of medicines supplied via homecare will be determined by a medicine-specific risk assessment during the commissioning of the homecare service. Refrigeration equipment that is correctly installed and maintained can still fail and equipment suppliers do not routinely accept liability for the loss of refrigerator contents due to equipment failure. Minimising stock holding by the patient and stock rotation will reduce the likelihood that any individual medicine is subject to storage outside 2 and 8$^{O}$C, and will minimise the impact of uncontrolled temperature excursions on those medicines.

The following risk factors will be considered:

### 4.1. Thermal stability and impact of temperature excursions on the medicine (see also section 6)

The following factors will be considered:

- Effects of elevated temperatures. Some medicines that require refrigerated storage have shelf lives up to three years from manufacture, while others (e.g. aseptically prepared OPAT medicines) may have shelf lives as short as a few days. A temperature excursion above 8$^{O}$C will therefore have a relatively greater impact on short shelf-life medicines than on long shelf-life medicines.
- Effects of freezing. Some medicines must not be subject to freezing. This may be because the medicine itself may be damaged by freezing, or it may be because the container may be damaged by freezing. Relatively brief periods of freezing may result in damage, so medicines labelled "do not freeze" may need more tightly controlled storage.

### 4.2. Quantities to be stored at one time, and the space they will occupy

The quantity and value of medicines to be supplied with each delivery, and the space that they will take up in the patient's home, needs to be considered when identifying the storage and monitoring requirements.

In some cases the quantity of stock will mean the patient needs to be provided with an additional refrigerator (See 5.3 below).

Limiting the quantities supplied to the minimum necessary will reduce the refrigeration capacity required and minimise the value of loss in the event of refrigeration equipment failure.

### 4.3. Ability to replace doses

The length of time that it would take to replace unusable doses, and the likelihood of missed doses (see also 4.4below), will be considered when choosing appropriate risk control measures.

### 4.4. Clinical consequence to patient of missing doses

The severity of the consequence of a missed dose, in the context of the likelihood of a missed dose occurring (see also above), will also be considered. Refer to clinical risk assessment page within the COVID-19 prescription management within homecare services exemplar risk assessment. *[https://www.sps.nhs.uk/articles/covid-19-prescription-management-exemplar-risk-assessment-national-homecare-medicines-committee/*

### 4.5. Value of stock

The impact of waste and replacement of high-cost stock will be considered.

## 5 Cold chain risk mitigation

Risk controls will be implemented to maintain patient safety; these will be commensurate with risks identified at risk assessment. Frequency of recording and reporting temperatures should be proportionate to the risk of temperature deviations on patient safety and potential for medicine wastage.

Implementation of unnecessarily complex risk controls increases difficulty for patients and increases equipment and maintenance costs. Furthermore, temperature monitoring and/or record keeping failures are likely to increase medicine wastage above those due to "real" temperature excursions.

Risk of wastage is increased if patient confidence is not maintained such that a patient is reluctant to use a medicine quarantined for investigation and later found to be usable. Once delivered to the patient home no medicines can be returned to stock and/or dispensed for another patient even if determined to be fit for use.

Risk controls will include some of the following, depending on the outcome of the risk assessment:

### 5.1. Provision of advice and training to patients about the correct storage of their "cold chain" medicines

In all cases written information will be provided to the patient regarding appropriate stock rotation and storage conditions of their homecare medicines. This will include instructions on timely transfer of cold chain homecare medicines into the refrigerator, and monitoring of the refrigerator's performance. Patients will always be instructed to report by exception if they believe their medicines have been subject to temperatures that are too high or too low or if their refrigerator has malfunctioned e.g. if the alarm sounds, the display reads below 2C or above 8C, or the refrigerator is unusually silent (see below: Table 1 Temperature excursion reporting only). The homecare team will take reasonable steps to ensure the patient understands their responsibilities to ensure the medicines are stored correctly in accordance with the instructions provided.

### 5.2. Storage in the patient's own domestic refrigerator

In most cases, medicines can be stored safely in the patient's own refrigerator, in the same way as patients would store medicines dispensed by community and hospital pharmacies, and no additional risk control measures will be required. The space required and available capacity within the patient's own refrigerator should be considered.

### 5.3. Provision of dedicated refrigeration equipment

If the patient's own refrigerator is unsuitable for storage of medicines, dedicated refrigeration equipment may need to be supplied via the homecare service. In all cases where refrigeration equipment is supplied it will be new or will have been subject to appropriate maintenance and testing according to the manufacturer's instructions prior to supply.

#### *5.3.1 Refrigeration Equipment choice*

Either Pharmacy or domestic refrigerators may be suitable. Several factors will be considered, taking into account the medicine and the patient's circumstances:

- Need for assisted air circulation to minimise hot and cold spots
- Need for integrated temperature monitoring and recording
- Need for the refrigerator to be lockable
- Ambient temperature operating conditions e.g. suitability for use in a garage or outbuilding
- Cost

If a domestic refrigerator is chosen, this should preferably be larder style without an ice box to reduce the likelihood of cold spots and to avoid the need to defrost regularly.

#### *5.3.2 Installation of Refrigeration Equipment*

- All refrigeration equipment provided as part of the homecare service will be installed, maintained and tested by a competent person in accordance with the manufacturer's instructions. Further advice can be obtained from the Health and Safety Executive https://www.hse.gov.uk/electricity/faq-portable-appliance-testing.htm
- If the refrigerator needs to settle before switching on, the installer will leave appropriate instructions for the patient or carer.
- Medicines will not be loaded into the newly installed refrigerator until the temperature has stabilised between 2$^{O}$C and 8$^{O}$C.

### 5.4. Temperature monitoring

There are several options for temperature monitoring (see Table 1). The mode of temperature monitoring implemented will be appropriate to the risks identified in the risk assessment:

- Too onerous or stringent requirements are inconvenient and time-wasting for the patient, and may result in more "alerts" than required to maintain patient safety and may undermine patient confidence and lead to increased wastage.
- Inadequate monitoring increases the risk that significant temperature excursions are not noticed.

Patients storing homecare medicines in their domestic refrigerator will always be instructed to report by exception if they believe their medicines have be subject to temperatures that are too hot or too cold - Table 1 Temperature excursion reporting only. Additional temperature monitoring will only be implemented where it provides a significant additional mitigating effect on temperature related risks.

Table 1 below compares a number of options that may be used in combination

**5.4.1 Table 1: Temperature monitoring options**

| Temperature monitoring system feature | Advantages | Disadvantages |
|---|---|---|
| **Temperature excursion reporting only** (no daily record kept) | • minimal impact on patient unless there is a temperature excursion | • relies entirely on patient reporting – no documentary evidence to provide assurance to the homecare team |
| **Manual temperature recording by patient** | • real time<br>• simple and inexpensive | • relies on patient to read and record accurately<br>• no record of out-of-limit events occurring in-between manual checks<br>• no temperature record showing extent and duration of temperature excursion |
| **Audible/visible temperature alarm** Refrigerators with this function have a continuous display of the current temperature, and have an audible alarm when the temperature goes out of range. | • real time<br>• simple system<br>• the current temperature is visible to the patient<br>• immediate action can be taken e.g. when the door is left open. | • display can only be read and alarm can only be heard when patient is in vicinity of refrigerator<br>• depends on patient reporting<br>• no record of out-of-limit events<br>• no temperature record showing extent and duration of temperature excursion |
| **Independent battery-operated max/min thermometer** These provide a continuous display of the current temperature and the maximum and minimum temperatures reached since the device was last reset. | • real time<br>• inexpensive<br>• relatively easy for patient to use and read<br>• the temperature is visible to the patient | • batteries need to be replaced periodically<br>• some training required to read temperatures and re-set after each reading<br>• requires action to read, reset by patient<br>• depends on patient reporting<br>• no temperature record showing extent and duration of temperature excursion |

| Temperature monitoring system feature | Advantages | Disadvantages |
|---|---|---|
| **Calibrated continuously recording data-logger with or without pre-set alarm lights** | • not normally patient readable (unless has pre-set alarm lights)<br>• facilitates retrospective determination of the extent and duration of a temperature excursion<br>• may be useful to reduce waste for very expensive product in case of temperature excursion reported via other means.<br>• no internet connection needed | • pre-set alarm lights show there has been an issue, but no details<br>• will normally need to be returned to the homecare team for download.<br>• if logger does not have human readable display excursions will not be detectable until downloaded so may need to be coupled with an alternative monitoring method<br>• expensive |
| **Calibrated continuously recording and transmitting data-logger** | • no need for patient to record temperatures<br>• facilitates real time determination by the homecare team of the extent and duration of a temperature excursion and initiate timely remedial action | • internet connection required<br>• the most expensive option – hardware, software and monitoring resources.<br>• homecare team needs to contact patient to agree corrective actions. |

Thermometers and data-loggers should be calibrated annually or in accordance with the manufacturer's instructions to ensure they function as intended.

Temperature monitoring probes should be carefully situated to ensure accurate and representative readings, preferably close to the homecare medicines. They should not touch the sides of the refrigerator, and care must be taken to ensure loose probes do not become trapped in the door or outside the refrigerator. Consideration should be given to situating the probe inside a mock product. This will buffer the probe from air temperature fluctuations and increase validity of the measurements.

## 6 Management of out-of-range temperature reports

Where temperatures are routinely monitored and/or reported, procedures will be in place to define the actions to be taken and when to escalate to a specialist pharmacist for further investigation. These procedures will be aligned with the homecare provider's in-house procedures for temperature excursions, and commensurate with the risks identified in Section 5 and should include:

- out-of-range temperature report
- deviations that are acceptable

- temperature report is not available

N.B. The evidence and information available to the pharmacist making individual decisions about individual temperature excursions may not be complete and professional judgment should always be exercised.

If there is disagreement between the parties involved in managing the temperature excursion, the parties will share information and risk assessments and work together to reach agreement on whether residual clinical risk arising from the incident is acceptable and the remedial actions to be implemented.

The following steps should be taken and it is important that all key information gathered and decisions taken are fully documented with reasons:

### 6.1. Take action to prevent risk of further damage to medicines, and to reassure the patient

Ascertain if the issue affects all or part of the medicine stock and, if appropriate and as a precaution, advise the patient to ensure affected stock is identifiable, e.g. kept physically separate from unaffected stock and/or to use an indelible pen to mark the boxes.

Assist the patient to return the medicines to the correct storage temperature, unless the patient has already done this. This could involve asking the patient to check that the refrigerator is plugged in and switched on, or asking them to temporarily transfer the medicines into an alternative refrigerator their own domestic or a neighbour's refrigerator whilst further investigations take place.

Reassure the patient, and ensure the patient is informed of any impact on their homecare service at all times.

### 6.2. Ensure continuity of patient treatment during investigation

In most cases any degradation of product integrity due to a temperature excursion occurring in the patient home will not be clinically significant. Where specific medicines have been identified as being at high risk of degradation due to incorrect storage, the patient may be advised to quarantine them i.e. to put to one side separate from any unaffected packs and not to use the affected packs until they receive further instruction. In this case, ensure the patient understands that this is precautionary whilst there is an investigation to confirm that the medicines are safe to use. The patient should be informed how long the investigation is expected to take and how they will be told about the outcome of the investigation.

Confirm when the patient's next dose is due. If their dose is due before the investigation outcome is expected, and the patient has insufficient usable doses, take all reasonable steps to ensure patient is provided with a supply of medicines to continue their treatment whilst the investigation takes place.

Additional information about minimising risks from missed doses is available from the NHS Specialist Pharmacy Service website:

https://www.sps.nhs.uk/articles/npsa-rapid-response-report-reducing-harm-from-omitted-and-delayed-medicines-in-hospital-a-tool-to-support-local-implementation/

https://www.sps.nhs.uk/articles/what-should-people-do-if-they-miss-a-dose-of-their-medicine/

### 6.3. Assess whether there is evidence that a "real" and significant temperature excursion has occurred

It is possible for out-of-range readings to occur, but for this to have no impact on the medicines. Apparent excursions may result if there is:

- failure in the monitoring method .e.g. failed battery; monitoring probe left outside refrigerator; probe touching the chiller panel.
- Air temperature excursion not impacting the product temperature. e.g. air temperature excursions between 8-25$^{O}$C of less than 20 minutes are unlikely to result in any significant warming of the medicine itself.

If there is insufficient evidence to conclude that a "real" temperature excursion may have occurred, arrange for repair/replacement of faulty monitoring equipment and/or arrange additional patient support in storing cold chain medicines and monitoring storage temperatures and continue from step **Error! Reference source not found.**. Otherwise, continue from step 6 .4.

### 6.4. Assess the likely impact of the temperature excursion on the product quality and patient safety

Where there is evidence that a real temperature excursion may have occurred consider:

- The storage requirements of the medicine including allowable time at room temperature (refer to SmPC, advice provided by the manufacturer (see below) or other published resources e.g. https://www.sps.nhs.uk/home/guidance/stability-outside-the-refrigerator ). N.B. medicines are expected to be handled at room temperature at some points in the life-cycle (e.g. dispensing and when collected from the community pharmacy and taken home), so some temperature excursions are expected.
- Duration of recorded temperature excursions e.g. short temperature excursions of less than 20 minutes are unlikely to be significant.
- The remaining shelf life of the product. For example, the product has a shelf life of 3 years of which 2 years are remaining and the patient will use the affected packs within 3 months. Despite the potential for accelerated deterioration, the quantity of active ingredient is likely to still be within expected limits at the point of administration unless the product is known to have exceptional thermal instability as noted in the SmPC.
- Is there risk that the product has slightly less active ingredient than expected and is this clinically significant?
- Is there any toxicity or hazard associated with degradation products associated with thermal decomposition of the product?
- If the medicine is known to have been subject to a previous temperature excursion the cumulative effect of the temperature excursions needs to be taken into account.
- Whether the product may have been frozen, even for a short time. Temperatures below 2$^{O}$C are unlikely to result in any significant degradation of the medicine unless the SmPC or manufacturer's storage information states "Do not freeze". Where this is the case, the risk assessment should seek to establish the freezing point of the product, the effect of freezing

on the product and its primary container and if there is a significant clinical risk arising if the product has been frozen.

**Seeking information from medicines manufacturers**

If, from the information available, the preliminary judgement of the person undertaking the investigation is that the product may not be safe to use, it may be helpful to contact the manufacturer directly, via the local pharmacy medicines information service or to use the SPS "Ask a question" service LNWH-tr.spsquestions@nhs.net before the final determination is made.

Note that manufacturers cannot recommend use of a licensed product that may have been stored outside its SmPC conditions, so simply asking whether a product can still be used is unlikely to elicit any helpful information. The manufacturer can only answer the specific question asked and cannot pro-actively provide additional information that they may have on file and may be useful to the investigation. It is recommended that the person undertaking the investigation should ask the manufacturer if they have any evidence of the product and/or active ingredient thermal stability or thermal instability relating to the specific conditions of the incident (or similar). A considered and structured direct question from a healthcare professional should elicit any additional information they manufacturer has "on file" to support the person undertaking the investigation to make their professional judgment. In some complex cases it may be useful to contact the manufacturer's QA team in addition to their Medical Information department.

If thermal instability is noted by the manufacturer the following information is important to aid the final determination.

- the speed of deterioration of the active ingredients under the conditions noted
- whether there is any known hazard from degradation products

If there is no evidence of a significant clinical risk to the patient from using the product and the person undertaking the investigation determines that the product is fit-for-use by the patient continue from step **Error! Reference source not found.**.

### 6.5. Remedial actions for a reported temperature excursion where the product can be used

In most cases, medicines will still be fit for use, with or without a reduced shelf life. In this case, the following actions will be taken or considered:

- Reassure the patient that the medicines are safe to use, and check that they are content to use the medicines.
- Ensure the patient understands they should use affected packs first either due to reduced shelf life or as a precautionary measure.
- Arrange for repair or replacement of failed refrigerator or monitoring equipment, if appropriate.
- Arrange additional patient support in storing cold chain medicines, if necessary.

### 6.6. Remedial actions for a significant temperature excursion where the Investigation finds the product is not safe to use

In some cases the investigation may conclude that some or all of the patient's stocks of medicines are not fit for the patient to use. In this case, the following actions will be taken or considered:

- Collect and/or arrange for destruction of affected medicines.
- Arrange for re-supply of replacement medicines unless clinically inappropriate to do so. Replacement of wasted medicines at the Purchasing Authority's expense may need prior authorisation by the relevant Purchasing Authority.
- Arrange for repair or replacement of failed refrigerator or monitoring equipment, if applicable.
- Ensure the patient understands and will follow any remedial actions.
- Arrange additional patient support for storing cold chain medicines correctly and monitoring storage temperatures.
- Record the wastage and report as agreed to the relevant Purchasing Authority.

### 6.7. Reporting and learning

Reporting and learning will be in accordance with Appendix 19 of the Homecare Handbook (Further Guidance on Managing Complaints and Incidents) https://www.rpharms.com/resources/professional-standards/professional-standards-for-homecare-services/appendix-19 This will consider:

- The number of doses that have been/could have been missed
- The clinical impact of missing a dose on the patient's clinical condition
- The impact of the incident on the patient's confidence in their care and treatment, or their ability to manage their homecare medicines
- Any previously unidentified risks
- The appropriateness of risk control measures in place for previously identified risks associated with the homecare services
- Sharing of learning across all organisations involved in the incident and/or homecare service
- Monitoring and reporting of trends and repeated incidents for UK wide learning initiatives

## 7 History

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## 8 Acknowledgements

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