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Review

# Stability of thermolabile drugs at room temperature. A review

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ABSTRACT

*Purpose:* The aim of this study was to review and compile the available information, in an easily accessible format, regarding the stability of thermolabile drugs at room temperature (22–25 °C), according to information contained in summary of product characteristics (SmPC), published literature, and information provided by the manufacturing pharmaceutical companies.

*Methods:* Drugs included in our hospital that required storage at a temperature between 2 and 8 °C were selected. Medications used in clinical trials, frozen drugs, and compounded formulations were excluded. The first source of information consulted for stability data was the SmPC. In case of no information available, published literature and gray literature were reviewed. If information was not found through these sources, the manufacturing laboratory was contacted.

The results are shown in table format to make the information more manageable. The table contains the following information: Drug product, trade name, brand name (manufacturer), maximum stability at room temperature, and information source. Stability data from SmPC were included for all medications, and for those with additional information obtained through the sources used in the study, this was included in a separate column.

*Results:* A total of 203 thermolabile drugs were selected. Thirty seven (18.2%) had a stability of 24 h at room temperature, 36 (17.7%) had a stability of 48 h–1 week, 63 (31%) had a stability of 1 week–1 month, and 52 (25.6%) had a stability of more than 1 month. However, 12 drugs (6.3%) had a stability of less than 24 h, and 3 drugs (1.4%) had other stability data at room temperature.

Stability information for 95 (46.7%) drugs was obtained from the SmPC, 56 (27.5%) from published literature, and 36 (26.2%) from manufacturers. In 21 of these cases, the stability information was valid exclusively for a specific case, with particular storage conditions and for a specific batch of the product.

*Conclusion:* The number and impact of thermolabile drugs have increased exponentially in recent years. The vast majority of these drugs maintain adequate stability at room temperature for an acceptable period of time, with some remaining stable for relatively long periods. To date, our study presents the largest dataset on the stability of these drugs. Therefore, the results of our study constitute a highly useful and up-to-date tool for saving time and money in hospital pharmacy units. Pharmaceutical manufacturers should consider publishing stability study results under non-recommended storage conditions in the SmPC.



## Estabilidad de los medicamentos termolábiles a temperatura ambiente. Revisión

*Palabras clave:*
Estabilidad de medicamento
Almacenamiento de medicamentos
Refrigeración
Producto Farmacéutico
Cadena frío

RESUMEN

*Objetivo:* El objetivo de este estudio fue revisar y aglutinar la información disponible, en un formato de fácil consulta, sobre la estabilidad de medicamentos termolábiles a temperatura ambiente (22–25 °C), de acuerdo a la ficha técnica, literatura publicada e información suministrada por los laboratorios fabricantes.

*Métodos:* Se seleccionaron los fármacos incluidos en nuestro hospital que debían almacenarse a una temperatura entre 2–8 °C. Se excluyeron los medicamentos utilizados en ensayos clínicos, los medicamentos congelados y las formulaciones magistrales. La primera fuente de información a la que se acudió para los datos de estabilidad fue la ficha técnica. En caso de no haber información disponible, consultamos literatura publicada y literatura gris. Si a través de estas fuentes no se encontraba la información, recurrimos al laboratorio fabricante.

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Los resultados son mostrados en formato tabla para hacer la información más manejable. La tabla contiene la siguiente información: principio activo, nombre comercial, fabricante, máxima estabilidad a temperatura ambiente, y fuente de información. Para todos los medicamentos se incluyó la información de estabilidad contenida en ficha técnica, y para aquellos de los que se disponía de información adicional obtenida a través de las fuentes utilizadas en el estudio, se incluyó en otra columna.

*Resultados:* Se seleccionaron 203 fármacos termolábiles. Treinta y siete (18,2%) tenían una estabilidad de 24 horas a temperatura ambiente, 36 (17,7%) medicamentos tenían una estabilidad de 48 horas a 1 semana, 63 (31%) de 1 semana a 1 mes y 52 (25,6%) tenían una estabilidad de más de 1 mes. Sin embargo 12 fármacos (5,9%), tenían una estabilidad de menos de 24 horas. Tres fármacos tenían una estabilidad a temperatura ambiente diferente.

La información de 95 (46,7%) medicamentos se obtuvo de la ficha técnica, la de 56 (27,5%) de literatura publicada, y la de los 52 restantes (25,6%) de los laboratorios. En 21 de estos casos, la información sobre la estabilidad del medicamento, era válida exclusivamente para un caso específico, con condiciones específicas de almacenamiento y para un determinado lote del producto.

*Conclusión:* El número e impacto de los medicamentos termolábiles se ha incrementado exponencialmente en los últimos años. La gran mayoría de ellos mantiene una estabilidad adecuada a temperatura ambiente durante un periodo aceptable de tiempo, y algunos durante periodos relativamente largos. Hasta la fecha, nuestro estudio es el que muestra datos de estabilidad para el mayor número de fármacos. Por tanto, los resultados de nuestro estudio constituyen una herramienta muy útil y actualizada, para ahorrar tiempo y dinero en las unidades de farmacia hospitalaria. Debería contemplarse que los laboratorios publiquen en las fichas técnicas los resultados de los estudios de estabilidad realizados fuera de las condiciones de almacenamiento recomendadas.



## Introduction

Thermolabile drugs represent a substantial portion of the pharmaceutical inventory in hospitals. These medications require storage within the cold chain, a series of logistical protocols designed to ensure that they are maintained at temperatures between 2 and 8 °C throughout storage, handling, transportation, and distribution.[1]

In clinical practice, unforeseen circumstances (e.g., power outages, cold-storage malfunctions, inadequate transportation, etc.) may disrupt the cold chain.[2] The storage conditions specified by the manufacturer and outlined in the summary of product characteristics (SmPC) ensure the stability, efficacy, and safety of the product until its expiration date. Disruptions in the cold chain can compromise the drug's properties to varying degrees, depending on the temperature reached and the duration of exposure. Additionally, such incidents may have significant economic repercussions for the healthcare system due to the high cost of many thermolabile drugs.[1,3]

According to Spanish legislation, Hospital Pharmacy departments are responsible for the custody and proper storage of drugs purchased by the facility.[4] Furthermore, a substantial proportion of medications dispensed to ambulatory patients by hospital pharmacies are thermolabile, and some studies suggest that these drugs frequently experience cold chain breaches post-dispensing.[5,6] Consequently, hospital pharmacies are often contacted by patients seeking information on the stability of these drugs following such incidents. For this reason, as well as the aforementioned factors, numerous publications have addressed this issue over the years.[7–10]

In recent decades, the development of new drugs—many of which are thermolabile—has increased exponentially. In many cases, data on the room temperature stability of drugs labeled for refrigeration is not available in the SmPC, necessitating a more in-depth search for information. The aim of this study was to provide updated information in an accessible format regarding the maximum stability of thermolabile drugs at room temperature, based on data from SmPCs, published literature, and information provided by pharmaceutical manufacturers.

## Methods

We selected all thermolabile drugs (requiring storage between 2 and 8 °C) stored at our hospital. Experimental drugs, frozen drugs, and compounded pharmaceutical formulations were excluded.

The primary source of stability data was the SmPC. If information regarding room temperature stability was not available in the SmPC, we consulted published literature from a preliminary exploratory search, described below. In cases where no data could be obtained through these sources, we contacted the manufacturer via telephone or email. We inquired about the maximum duration for which the drug could remain stable at room temperature or, alternatively, whether it could remain stable for at least 24 h under these conditions.

In several instances, the information provided referred to specific cases of storage errors that had occurred within our department prior to this study. In these situations, we requested details on the specific conditions of the storage error (e.g., storage of a medication at temperatures above 8 °C for 18 h, reaching a maximum of 17 °C). These particular cases may not be entirely generalizable to other situations.

The literature search mentioned above was an exploratory search conducted in the MEDLINE database using the terms “Freezing,” “Stability,” “Thermolabile drugs,” and “Cold chain,” without restrictions on publication years. Given that information on this topic is often found in gray literature (hospital guidelines, documents from professional societies, conference abstracts, online repositories, etc.), we also conducted searches using the same terms in Google and Google Scholar databases.

We collected the following data: drug product, trade name, manufacturer, acceptable duration of storage at room temperature, and source of information. To improve usability, we compiled a table summarizing the stability data (Table 1. Acceptable duration of room-temperature storage for medications labeled for refrigeration). This table includes stability information from the SmPC and, when available, data from other sources.

## Results

We selected 203 thermolabile drugs which are showed in Table 1.

Among these drugs, 37 (18.2%) exhibited stability for 24 h at room temperature, 36 (17.7%) showed stability for 48 h to 1 week, 63 (31%) had stability between 1 week and 1 month, and 52 (25.6%) maintained stability for 1 month or more. Conversely, 12 drugs (5.9%) demonstrated stability of less than 24 h. Finally, 3 drugs (1.4%) had other stability data at room temperature.

Information for 95 of the 203 thermolabile drugs (46.7%) was obtained from the SmPC. The stability data for 56 (27.5%) drugs were

**Table 1**
Storage information for medications labeled for refrigeration.

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Adalimumab and biosimilars medicines | 20 mg, 40 mg and 80 mg solution for injection in pre-filled syringe/pen, different brand names | Different manufacturers | Between 14 and 31 days ≤25 °C, depending on biosimilar | No additional stability data | SmPC |
| Aflibercept | Eylea 40 mg/ml solution for injection in pre-filled syringe. | Bayer | 24 h at ≤25 °C | No additional stability data | SmPC |
| Aflibercept | Zaltrap 25 mg/ml concentrate for solution for infusion | Sanofi | 8 h at ≤25 °C | No additional stability data | SmPC |
| Agalsidase alfa | Replagal 1 mg/ml concentrate for solution for infusion | Takeda Pharmaceuticals International | Keep at 2–8 °C | 45 days between 8 and 27 °C | Mateo *et al.* (2017) |
| Agalsidase beta | Fabrazyme 5 mg and 35 mg powder for concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 6 months between 23 and 27 °C | Mateo *et al.* (2017) |
| Aldesleukin | Proleukin 18 MIU powder for solution for injection | Novartis | 48 h at ≤30 °C | No additional stability data | SmPC |
| Alemtuzumab | Lemtrada 12 mg concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 1 month at 30 ± 2 °C and 3 months at 25 ± 2 °C | Mateo *et al.* (2017) |
| Alglucosidase | Myozyme 50 mg powder for concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 6 months between 23 and 27 °C | Mateo *et al.* (2017) |
| Alirocumab | Praluent 75 mg, 150 mg, and 300 mg solution for injection in pre-filled pen/syringe | Sanofi | 1 month at ≤25 °C | No additional stability data | SmPC |
| Alprostadil | Alprostadil 0.5 mg/ml solution for injection | Pfizer | Keep at 2–8 °C | 4 months at ≤25 °C | Manufacturer |
| **Amivantamab**[a] | **Rybrevant 350 mg concentrate for solution for infusion** | **Janssen** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Amphotericin B | Abelcet lipid complex concentrate for solution for infusion | Teva Pharma | Keep at 2–8 °C | Each day of storage at 25 °C is equivalent to 9 days at 5 °C | Mateo *et al.* (2017) |
| Anakinra 100 mg/ 0.67 ml INJ | Kineret 100 mg/0.67 ml solution for injection in pre-filled syringe | Swedish Orphan Biovitrum | 72 h at ≤25 °C | No additional stability data | SmPC |
| Anidulafungin 100 mg INJ | Ecalta 100 mg powder for concentrate for solution for infusion | Normon | 4 days at ≤25 °C | No additional stability data | SmPC |
| Anti-D Immunoglobulin 750 IU/ml INJ | Igamad 750 UI/ml solution for injection in pre-filled syringe | Grifols | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Atracurium 50 mg INJ | Tracrium 10 mg/ml solution for injection or infusion | Aspen Pharmacare | For transport or temporary storage, short periods of up to 25° are allowed. A 5% loss of potency may occur if Tracrium is stored at 25 °C for 1 month | No additional stability data | SmPC |
| Axicabtagen ciloleucel | Yescarta 0.4–2 × 108 cells dispersion for infusion | Kite Pharma | Once completely thawed, stable for up to 3 h at room temperature (20–25 °C). However, the infusion should be started within 30 min of complete thawing, and the total infusion time of Yescarta should not exceed 30 min. The product should not be refrozen once thawed | No additional stability data | SmPC |
| Aztreonam | Cayston 75 mg powder and solvent for nebulizer solution | Gilead Sciences | 28 days at ≤25 °C | 2 months at ≤25 °C | Mateo *et al.* (2017) |
| Beclometasone/ Formoterol/ Glycopyrronium | Trimbow 87/5/9 mcg pressurized inhalation, solution. 120 and 180 actuation pressurized container | Chiesi | 4 months at ≤25 °C | No additional stability data | SmPC |
| Beclometasone/ Formoterol/ Glycopyrronium | Trimbow 87/5/9 mcg pressurized inhalation, solution. 60 actuation pressurized container | Chiesi | 2 months at ≤25 °C | No additional stability data | SmPC |
| Belimumab | Benlysta 120 mg and 400 mg powder for solution for injection | GlaxoSmithKline | Keep at 2–8 °C | 21 days at ≤25 °C | Manufacturer |
| Belimumab | Benlysta 200 mg solution for injection in pre-filled pen | GlaxoSmithKline | 12 h at ≤25 °C | No additional stability data | SmPC |
| Benralizumab | Fasenra 30 mg solution for injection in pre-filled syringe/pen | AstraZeneca | 14 days at ≤25 °C | No additional stability data | SmPC |
| Beta-glucuronidase | Mepsevii 2 mg/ml concentrate for solution for infusion | Ultragenyx | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Bevacizumab | Avastin 25 mg/ml concentrate for solution for infusion | Roche | Keep at 2–8 °C | 5 days between 15 and + 30 °C and 9 h at ≤30 °C | Mateo *et al.* (2017) |
| Bleomycin Sulfate | Bleomycin 15.000 UI (Ph. Eur.) = 15 U (USP) powder for solution for injection | Mylan Pharmaceuticals | Keep at 2–8 °C | 28 days at ≤25 °C | Mateo *et al.* (2017) |
| Botulinum Toxin Type A 2500 IU INJ | NeuroBloc 2500 UI/ml, 5000 U/ml and 10 000 IU/ml solution for injection | Sloan Pharma | 3 months at ≤25 °C | No additional stability data | SmPC |

(continued on next page)

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Botulinum Toxin Type A 50 IU,100 IU INJ | Botox 50 UI, 100 UI, and 200 UI powder for solution for injection | Abbvie | Keep at 2–8 °C | 14 days at a temperature up to 25 °C (only once); 7 days at a temperature up to 30 °C (only once; store in refrigerator (2–8 °C), or in freezer (at a temperature of −5 °C or lower). | Mateo *et al.* (2017) |
| Botulinum Toxin Type A 500 IU INJ | Dysport 500 UI powder for solution for injection | Ipsen Pharma | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Brentuximab 50 mg INJ | Adcentris 50 mg powder for concentrate for solution for infusion | Takeda Pharmaceuticals International | Keep at 2–8 °C | 14 days at ≤25 °C | Mateo *et al.* (2017) |
| Brodalumab | Kyntheum 210 mg solution for injection in pre-filled syringe | Leo Pharma | 14 days at ≤25 °C | No additional stability data | SmPC |
| Burosumab | CRYSVITA 10 mg, 20 mg, and 30 mg solution for injection | Kyowa Kirin | Keep at 2–8 °C | 21 h at ≤25 °C | Manufacturer |
| Calcitonin | Calcitonin 100 UI/ml solution for injection | Almirall | Keep at 2–8 °C | 1 month at ≤22°C | Mateo *et al.* (2017) |
| Cannabidiol | Sativex 2.7 mg/2.5 mg oromucosal spray | Jazz Pharmaceuticals | Keep at ≤25 °C (open) | 42 days at ≤25 °C | Ricote-Lobera *et al.* (2013) |
| Caplacizumab | Cablivi 10 mg powder and solvent for solution for injection | Ablynx | 2 months at ≤25 °C | No additional stability data | SmPC |
| **Casirivimab**[a] | **Ronapreve 300 mg + 300 mg solution for injection/infusion** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Caspofungin | Caspofungin 50 mg and 70 mg powder for solution for infusion | Lorien | Keep at 2–8 °C | 7 days at ≤25 °C and 3 days at ≤30 °C | Manufacturer |
| **Ceftolozane/ tazobactam**[a] | **Zerbaxa 1 g/0.5 g powder for concentrate for solution for infusion** | **Merck** | **Keep at 2–8 °C** | **48 h at ≤25 °C** | **Manufacturer** |
| **Cemiplimab**[a] | **Libtayo 350 mg concentrate for solution for infusion** | **Regeneron Pharmaceuticals** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Certolizumab pegol | Cimzia 200 mg solution for injection in pre-filled syringe | UCB Pharma | 10 days at ≤25 °C | No additional stability data | SmPC |
| Cetuximab | Erbitux 5 mg/ml solution for infusion, vials of 100 mg and 500 mg | Merck | Keep at 2–8 °C | 20 h at ≤25 °C | Bovaira *et al.* (2004) |
| Chorionic gonadotropin | Ovitrelle 250 µg/0.5 ml solution for injection in pre-filled syringe | Merck | Keep at 2–8 °C | 1 month at ≤25 °C | Mateo *et al.* (2017) |
| Cisatracurium | Cisatracurium 2 mg/ml and 5 mg/ml solution for injection/infusion. | Laboratorios Reig Jofre | 21 days at ≤25 °C | No additional stability data | SmPC |
| Clevidipine | Cleviprex 0.5 mg/ml emulsion for injection | Ferrer | Keep at 2–8 °C | 2 months at ≤25 °C | Mateo *et al.* (2017) |
| Damoctocog alfa pegol | Jivi 250 IU, 500 IU, 1000 IU, 2000 IU, and 3000 IU powder and solvent for solution for injection | Bayer | 6 months at ≤25 °C | No additional stability data | SmPC |
| Darbepoetin alfa | Aranesp 10 mcg, 15 mcg, 20 mcg, 30 mcg, 40 mcg, 50 mcg, 60 mcg, 80 mcg, 100 mcg, 130 mcg, 150 mcg, 300 mcg, and 500 mcg solution for injection in pre-filled syringe, pen and vial | Amgen | 7 days at ≤25 °C | No additional stability data | SmPC |
| Denosumab | Xgeva 120 mg solution for injection Prolia 60 mg solution for injection in pre-filled syringe | Amgen | 1 month at ≤25 °C | No additional stability data | SmPC |
| Desmopressin | Minurin 0.1 mg/ml inhalation solution | Ferring Pharmaceuticals | Keep at 2–8 °C | 7 days at ≤24.5°(close); 1 month at ≤25° (open) | Ricote-Lobera *et al.* (2013) |
| Desmopressin | Minurin 4 mcg solution for injection | Ferring Pharmaceuticals | Keep at 2–8 °C | 24 h at ≤25 °C | Ricote-Lobera *et al.* (2013) |
| Dinoprostone | Prostaglandin E2 10 mg/ml concentrate for solution for infusion | Pfizer | Keep at 2–8 °C | 15 days at ≤25 °C | Manufacturer |
| Dinoprostone | Prostin E2 0.5 mg vaginal tablets | Pfizer | Keep at 2–8 °C | 1 month at ≤25 °C | Mateo *et al.* (2017) |
| Dinutuximab[a] | Qarziba 4.5 mg/ml concentrate for solution for infusion | Recordati | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| **Diphtheria-tetanus vaccine**[a] | **Diftavax suspension for injection.** | **Sanofi** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Diphtheria-tetanus-pertussis vaccine | Triaxis suspension for injection | Sanofi | 72 h at ≤25 °C | No additional stability data | SmPC |
| Diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenzae* type b vaccin | Infanrix hexa, powder and suspension for injection | GlaxoSmithKline | 72 h at ≤25 °C | No additional stability data | SmPC |
| Dornase alfa | Pulmozyme 2500 U/2.5 ml, nebulizer solution | Roche | 24 h at ≤30 °C | 71 h at ≤30 °C. Maximum 5 cycles of congelation | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Doxorubicin liposomal | Myocet liposomal 50 mg powder, dispersion and solvent for concentrate for dispersion for infusion | Teva Pharma | Keep at 2–8 °C | 2 years at ≤25 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |
| Doxycycline | Vibravenosa 100 mg solution for injection | Pfizer | Keep at 2–8 °C | 1 month at ≤25 °C | Mateo et al. (2017) |
| DTaP-IPV-HepB-Hib vaccine | Hexyon suspension for injection in pre-filled syringe | Pfizer | Keep at 2–8 °C | 72 h at ≤25 °C | Manufacturer |
| Dupilumab | Dupixent 200 mg and 300 mg solution for injection in pre-filled syringe and pen | Sanofi | 14 days at ≤25 °C | No additional stability data | SmPC |
| Durvalumab | Imfinzi 50 mg/ml concentrate for solution for infusion | AstraZeneca | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Eculizumab | Soliris 300 mg concentrate for solution for infusion | Alexion Europe | 72 h at ≤25 °C | No additional stability data | SmPC |
| Emicizumab | Hemlibra 30 mg/ml and 150 mg/ml solution for injection | Roche | 7 days at ≤30 °C | No additional stability data | SmPC |
| Epirubicin hydrochloride | Epirubicin hydrochloride 2 mg/ml solution for injection | Accord Healthcare | Keep at 2–8 °C | 72 h at ≤25 °C | Mateo *et al.* (2017) |
| Epoetin alfa | Binocrit 1000 IU/0.5 ml, 2000 IU/1 ml, 3000 IU/0.3 ml, 4000 IU/0.4 ml, 5000 IU/0.5 ml, 6000 IU/0.6 ml, 7000 IU/0.7 ml, 8000 IU/0.8 ml, 9000 IU/0.9 ml, 10 000 IU/1 ml, 20 000 IU/0.5 ml, 30 000 IU/0.75 ml and 40 000 IU/1 ml solution for injection in a pre-filled syringe | Sandoz | 72 h at ≤25 °C | No additional stability data | SmPC |
| Epoetin beta | NeoRecormon 500 IU, 2000 IU, 3000 IU, 4000 IU, 5000 IU, 6000 IU, 10 000 IU, 20 000 IU, 30 000 IU solution for injection in pre-filled syringe | Roche | 72 h at ≤25 °C | No additional stability data | SmPC |
| Epoetin zeta | Eporatio 1000 IU/0.5 ml, 2000 IU/0.5 ml, 3000 IU/0.5 ml, 4000 IU/0.5 ml, 5000 IU/0.5 ml, 10 000 IU/1 ml, 20 000 IU/1 ml and 30 000 IU/1 ml solution for injection in pre-filled syringe | Ratiopharm | 7 days at ≤25 °C | No additional stability data | SmPC |
| Erenumab | Aimovig 70 mg and 140 mg solution for injection in pre-filled syringe and pen | Novartis | 7 days at ≤25 °C | No additional stability data | SmPC |
| Etanercept | Enbrel 25 mg powder for solution for injection | Pfizer | 1 month at ≤25 °C | No additional stability data | SmPC |
| Etanercept | Erelzi 25 mg, 50 mg solution for injection in pre-filled syringe and pen | Sandoz | 1 month at ≤25 °C | No additional stability data | SmPC |
| Etelcalcetide 2.5 mg, 5 mg, 10 mg INJ | Parsabiv 2.5 mg, 5 mg, 10 mg solution for injection | Amgen | 7 days at ≤25 °C | No additional stability data | SmPC |
| Evolocumab | Repatha 140 mg solution for injection in pre-filled syringe and pen | Amgen | 1 month at ≤25 °C | No additional stability data | SmPC |
| Factor IX | Factor IX 50 IU/ml powder for solution for injection | Grifols | Keep at 2–8 °C | 3 months at ≤40 °C | Mateo *et al.* (2017) |
| Factor VIII | Cluvot 250 IU and 1250 IU, powder for solution for injection | CSL Behring | Keep at 2–8 °C | 48 h at ≤25 °C | Manufacturer |
| Filgrastim | Accofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe | Accord Healthcare | Keep at 2–8 °C | 15 days at ≤25 °C | Mateo *et al.* (2017) |
| **Fludarabine**[a] | **Beneflur 25 mg/ml solution for injection/infusion** | **Sanofi** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Fluorescein sodium + Oxybuprocaine | Colircusi Fluotest 20 mg/ml eye drops, solution | Alcon Cusi | Keep at 2–8 °C | 15 days at ≤25 °C | Mateo *et al.* (2017) |
| Fotemustine | Mustoforan 50 mg/ml powder and solvent for solution for infusion | Servier | Keep at 2–8 °C | 10 weeks at ≤25 °C | Ricote-Lobera *et al.* (2013) |
| Gemtuzumab ozogamicin | Mylotarg 5 mg powder for concentrate for solution for infusion | Pfizer | Keep at 2–8 °C | 4 days at ≤25 °C | Manufacturer |
| Fremanezumab | Ajovy 225 mg solution for injection in pre-filled syringe and pen | Teva Pharma | 7 days at ≤30 °C | No additional stability data | SmPC |
| Fulvestrant | Faslodex 250 mg solution for injection | AstraZeneca | 28 days at ≤25 °C | No additional stability data | SmPC |
| Galcanezumab | Emgality 120 mg solution for injection in pre-filled pen | Lily | 7 days at ≤30 °C | No additional stability data | SmPC |
| Glatiramer | Glatiramer 20 mg/ml and 40 mg/ml solution for injection in pre-filled syringe | Viatris | 1 montch at ≤25 °C. | No additional stability data | SmPC |

(*continued on next page*)

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Golimumab | Simponi 50 mg/0.5 ml and 100 mg/ml solution for injection in pre-filled pen | Janssen | 1 month at ≤25 °C | No additional stability data | SmPC |
| Gonadorelin | Gonadorelin 100 mcg solution for injection | Ferring Pharmaceuticals | Keep at 2–8 °C | 15 days at ≤25 °C | Periáñez *et al.* (2011) |
| **Guselkumab**[a] | **Tremfya 100 mg solution for injection in pre-filled syringe and pen** | **Janssen** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Hemin | Normosang 25 mg/ml, concentrate for solution for infusion | Recordati | Keep at 2–8 °C | 7 days at ≤25 °C | Mateo *et al.* (2017) |
| Hepatitis A and B adult or pediatric vaccine | Twinrix, suspension for injection in pre-filled syringe | GlaxoSmithKline | Keep at 2–8 °C | 14 days at ≤21 °C and 7 days at ≤37 °C | Ricote-Lobera *et al.* (2013) |
| Hepatitis B surface antigen | Fendrix suspension for injection | GlaxoSmithKline | Keep at 2–8 °C | 7 days at ≤25 °C and 48 h at ≤37°C | Manufacturer |
| Hepatitis A vaccine | Havrix, suspension for injection in pre-filled syringe | GlaxoSmithKline | 72 h at ≤25 °C | No additional stability data | SmPC |
| Hepatitis B virus infection vaccine | Engerix-B 20 µg/1 ml suspension for injection in pre-filled syringe | GlaxoSmithKline | 7 days ≤25 °C and 72 h at ≤37 °C | No additional stability data | SmPC |
| Herpes zoster vaccine | Shingrix powder and suspension for suspension for injection | GlaxoSmithKline | Keep at 2–8 °C | 7 days ≤30 °C. | Manufacturer |
| Human Hepatitis B Immunoglobulin | Igantibe 200 IU/ml solution for injection | Grifols | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Human Hepatitis B Immunoglobulin | Niuliva 250 IU/ml solution for infusion | Grifols | Keep at 2–8 °C | 6 months at ≤30 °C | Mateo *et al.* (2017) |
| Human papillomavirus vaccine | Gardasil suspension for injection in a pre-filled syringe | Merck | 72 h at ≤42 °C | No additional stability data | SmPC |
| Human Varicella-Zoster Immunoglobulin | Varitect 25 IU/ml solution for infusion | Biotest | Keep at 2–8 °C | 72 h at ≤25 °C | Ricote-Lobera *et al.* (2013) |
| Idarubicine | Zavedos 5 mg and 10 mg powder for concentrate for solution for infusion | Pzifer | 24 h at ≤25 °C | No additional stability data | SmPC |
| Idursulfase | Elaprase 2 mg/ml concentrate for solution for infusion | Takeda Pharmaceuticals International | 8 h at ≤25 °C | No additional stability data | SmPC |
| Imiglucerase | Cerezyme 400 IU powder for concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 7 days between 23 and 25 °C | Mateo *et al.* (2017) |
| Immunoglobulin | Igamplia 160 mg/ml solution for injection | Grifols | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Inotuzumab ozogamicin | Besponsa 1 mg powder for concentrate for solution for infusion | Pfizer | Keep at 2–8 °C | 1 year at ≤25 °C | Manufacturer |
| Insulin aspart | NovoRapid 100 IU/ml solution for injection in vial, cartridge and pre-filled pen | Novo Nordisk | 24 h ≤25 °C (close); 4 weeks at ≤30 °C (open) | No additional stability data | SmPC |
| lnsulin aspart/ protamine-crystallized + insulin aspart | Novomix 100 IU/ml suspension for injection in cartridge and pre-filled pen | Novo Nordisk | 24 h ≤25 °C (close); 4 weeks at ≤30 °C (open) | No additional stability data | SmPC |
| Insulin detemir | Levemir 100 IU/ml solution for injection in cartridge and pre-filled pen | Novo Nordisk | 24 h ≤25 °C (close); 4 weeks at ≤30 °C (open) | No additional stability data | SmPC |
| Insulin glargine | Abasaglar 100 IU/ml solution for injection in a cartridge | Lilly | 28 days at ≤30 °C (open) | No additional stability data | SmPC |
| Insulin glargine | Toutejo 300 IU/ml solution for injection in a pre-filled pen | Sanofi | 6 weeks at ≤30 °C (open) | No additional stability data | SmPC |
| Insulin glulisine | Apidra 100 IU/ml solution for injection in a vial, cartridge, and pre-filled pen | Sanofi | 1 month at ≤25 °C | No additional stability data | SmPC |
| Insulin lispro + insulin lispro protamine | Humalog mix 100 IU/ml solution for injection in vial, cartridge, and pre-filled pen | Lilly | 28 days after first use at ≤30 °C | No additional stability data | SmPC |
| Insulin lispro | Humalog 100 IU/ml and 200 IU/ml solution for injection in vial, cartridge, and pre-filled pen | Lilly | 28 days after first use at ≤30 °C | No additional stability data | SmPC |
| Interferon alfa-2a | Roferon-A 9 million IU solution for injection in prefilled syringe | Roche | Keep at 2–8 °C | 6 days and 21 h at ≤25° | Mateo *et al.* (2017) |
| Interferon alfa-2b | Bioferon 5 million IU solution for injection in prefilled syringe | Alba | Keep at 2–8 °C | 7 days at ≤25°C | Manufacturer |
| Interferon beta-1a | Rebif 22 mcg and 44 mcg solution for injection in pre-filled syringe | Merck | 14 days at ≤25°C | No additional stability data | SmPC |
| Interferon beta-1a | Avonex 30 µg/0.5 ml solution for injection | Biogen | 7 days at ≤30 °C | No additional stability data | SmPC |
| Ipilimumab | Yervoy 5 mg/ml concentrate for solution for infusion | Bristol-Myers Squibb | Keep at 2–8 °C | 48 h at ≤25 °C | Manufacturer |

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Irinotecan pegylated liposomal | Onivyde pegylated liposomal 4.3 mg/ml concentrate for dispersion for infusion | Servier | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| **Isatuximab**[a] | **Sarclisa 20 mg/ml concentrate for solution for infusion** | **Sanofi** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Isavuconazole | Cresemba 200 mg powder for concentrate for solution for infusion | Pfizer | Keep at 2–8 °C | 90 h at ≤25 °C | Manufacturer |
| Isophane human insulin (NPH) | Humulin NPH 100 IU/ml, suspension for injection in vial | Lilly | Keep at ≤30 °C (open) | 14 days ≤10 °C; 7 days ≤15 °C; 4 days ≤20 °C; 48 h ≤25 °C; 24 h ≤30 °C; 12 h ≤35 °C; 6 h ≤45 °C (close). 28 days at ≤30 °C (open) | Mateo *et al.* (2017) |
| **Isoprenaline chlorhydrate**[a] | **Aleudrin 0.2 mg/ml solution for injection** | **Laboratorios Reig Jofre** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Ixekizumab | Taltz 80 mg solution for injection in pre-filled syringe | Lilly | 5 days at ≤30 °C | No additional stability data | SmPC |
| Leuprorelin acetate | Eligard 22.5 and 45 mg powder and solvent for solution for injection | Recordati | 4 weeks at ≤25°C | No additional stability data | SmPC |
| Laronidase | Aldurazyme 100 IU/ml concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 6 months at 25 ± 2 °C and 2 months at 37 ± 2 °C or 40 ± 2 °C | Mateo *et al.* (2017) |
| Levosimendan | Simdax 2.5 mg/ml concentrate for solution for infusion | Ever Pharma | Keep at 2–8 °C | 24 h at ≤25 °C and 48 h at ≤15 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |
| **Levothyroxine**[a] | **500 mcg powder and solvent for solution for injection** | **Sanofi** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Lonoctocog alfa | Afstyla 250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU, 2500 IU, and 3000 IU powder and solvent for solution for injection | CSL Behring | 3 months for a single period at ≤25 °C. Do not refrigerate again | No additional stability data | SmPC |
| Meningococcal C vaccine | Neisvac C suspension for injection in pre-filled syringe | Pfizer | 9 months ≤25 °C | No additional stability data | SmPC |
| Meningococcal A, C, W-135 and Y vaccine | Nimenrix powder and solvent for solution for injection in pre-filled syringe | Pfizer | Keep at 2–8 °C | 7 days at ≤37 °C | Mateo *et al.* (2017) |
| Meningococcal group B vaccine | Bexsero suspension for injection in pre-filled syringe | GlaxoSmithKline | Keep at 2–8 °C | 48 h at ≤25 °C | Manufacturer |
| Mepolizumab | Nucala 100 mg solution for injection in pre-filled pen/syringe | GlaxoSmithKline | 7 days at ≤30 °C in the unopened package. After opening the package, it is stable for 8 h. | No additional stability data | SmPC |
| Methylergonovine | Methergin 0.2 mg/ml solution for injection | Novartis | 14 days at ≤25°C | No additional stability data | SmPC |
| Moroctocog alfa | Refacto 250 IU, 500 IU, 1000 IU, 2000 IU, and 3000 IU INJ powder and solvent for solution for injection in pre-filled syringe | Pfizer | 3 months at ≤25 °C | No additional stability data | SmPC |
| Mifamurtide | Mepact 4 mg powder for concentrate for dispersion for infusion | Takeda Pharmaceuticals International | Keep at 2–8 °C | 6 days at ≤40 °C | Mateo *et al.* (2017) |
| **Natalizumab**[a] | **Tysabri 300 mg concentrate for solution for infusion** | **Biogen** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Nitisinone | Orfadin 2 mg, 5 mg, 10 mg, and 20 mg hard capsules | Swedish Orphan Biovitrum | 2 months at ≤25 °C (2 mg); 3 months at ≤25 °C (5 mg, 10 mg, 20 mg) | No additional stability data | SmPC |
| Nivolumab | Opdivo 10 mg/ml concentrate for solution for infusion | Bristol-Myers Squibb | 48 h at ≤25 °C | No additional stability data | SmPC |
| Nonacog beta pegol | Refixia 500 IU, 1000 IU, 2000 IU, and 3000 IU powder and solvent for solution for injection | Novo Nordisk | 1 year for a single period at ≤30 °C. Do not refrigerate again | No additional stability data | SmPC |
| Nusinersen | Spinraza 12 mg solution for injection | Biogen Netherlands | 14 days at ≤30 °C in the original packaging. Out of original packaging, 30 h at ≤25°C | No additional stability data | SmPC |
| **Obinutuzumab**[a] | **Gazyvaro 1000 mg concentrate for solution for infusion** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| **Ocrelizumab**[a] | **Ocrevus 300 mg concentrate for solution for infusion** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Octocog alfa | Advate 250 IU, 500 IU,1000 IU, and 2000 IU INJ powder and solvent for injectable solution | Takeda Pharmaceuticals International | 6 months at ≤25 °C. Do not refrigerate again | No additional stability data | SmPC |
| Octreotide | Octreotide 0.05 mg/ml, 0.1 mg/ml, 0.5 mg/ml, and 0.2 mg/ml solution for injection or infusion | Gp Pharm | Keep at <5 °C | 72 h at ≤25 °C | Ricote-Lobera *et al.* (2013) |
| Octreotide | Sandostatin 10 mg, 20 mg, and 30 mg powder and solvent for injectable suspension | Novartis | Keep at 2–8 °C | 14 days at ≤25 °C | Ardanaz (2008) |

(*continued on next page*)

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Omalizumab | Xolair 75 mg and 150 mg solution for injection in pre-filled syringe | Novartis | 48 h at ≤25 °C | No additional stability data | SmPC |
| Onko BCG | 100 mg powder for injectable suspension | Biopharmed Iberica | Keep at 2–8 °C | 4 h at ≤8 °C | Manufacturer |
| Palivizumab | Synagis 50 mg and 100 mg solution for injection | AstraZeneca | Keep at 2–8 °C | 14 days at ≤25 °C and 4 days at ≤40 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |
| Panitumumab | Vectibix 100 mg and 400 mg concentrate for solution for infusion | Amgen | Keep at 2–8 °C | 48 h at ≤20 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |
| Calcium patiromer | Veltassa 8.4 g, 16.8 g, and 25.2 g powder for oral suspension | Vifor Fresenius Medical Care Renal Pharma | 6 months at ≤25 °C | No additional stability data | SmPC |
| Patirisan | Onpattro 10 mg concentrate for solution for infusion | Alnylam Netherlands B.V. | 14 days at ≤25 °C | No additional stability data | SmPC |
| Pegaspargase | Oncaspar 750 IU/ml powder for solution for injection | Servier | Keep at 2–8 °C | 48 h at ≤25 °C | Mateo *et al.* (2017) |
| Pegfilgrastim | Ziextenzo 6 mg solution for injection in pre-filled syringe | Sandoz | 5 days at ≤30°C | No additional stability data | SmPC |
| Peginterferon beta-1a | Plegridy 125 mcg and 63/94 mcg solution for injection in pre-filled syringe | Biogen | 1 month at ≤25 °C | No additional stability data | SmPC |
| Pembrolizumab | Keytruda 50 mg and 100 mg powder for concentrate for solution for infusion | Merck | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| **Pertuzumab**[a] | **Perjeta 420 mg powder for concentrate for solution for infusion** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Plasminogen/ Thrombin/Human fibrinogen/Human Factor XIII | Tisseel 800 mcg, 500 IU, 90 mg, and 30 IU solutions for sealant | Baxter | 72 h at ≤25 °C. Store frozen at ≤−20 °C | No additional stability data | SmPC |
| Pneumococcal polysaccharide vaccine 13 | Prevenar 13 suspension for injection | Pfizer | 4 days at ≤25 °C | No additional stability data | SmPC |
| Pneumococcal polysaccharide vaccine 23[a] | Pneumovax 23 solution for injection in pre-filled syringe | Merck | Keep at 2–8 °C | 12 h at ≤25 °C | Manufacturer |
| **Polatuzumab**[a] | **Polivy 140 mg powder for concentrate for solution for infusion** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Porcine surfactant | Curosurf 120 mg and 240 mg endotracheopulmonary instillation suspension | Chiesi | 24 h at ≤25 °C. Do not freeze again | No additional stability data | SmPC |
| Posaconazole | Noxafil 300 mg oral suspension | Merck | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Rabbit antithymocyte globulin | Rabbit antithymocyte globulin 5 mg/ml powder for concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 12 months at 25 ± 2 °C | Mateo *et al.* (2017) |
| Ranibizumab | Lucentis 10 mg/ml solution for injection | Novartis | 24 h at ≤25 °C | No additional stability data | SmPC |
| Rasburicase | Fasturtec 1.5 mg powder and solvent for concentrate for solution for infusion | Sanofi | Keep at 2–8 °C | 15 days at ≤25 °C. Do not freeze again | Mateo *et al.* (2017) |
| Risankizumab | Skyrizi 75 mg and 150 mg solution for injection in pre-filled syringe/pen | Abbvie | 24 h at ≤25 °C. | No additional stability data | SmPC |
| Risperidone | Risperdal 25 mg, 37.5 mg, and 50 mg powder and solvent for prolonged-release suspension for injection | Janssen | 7 days at ≤25 °C | No additional stability data | SmPC |
| Ritonavir + lopinavir | Kaletra 80 + 20 mg/ml oral solution | Abbvie | 6 weeks at ≤25 °C. 24 h between 26 and 30 °C. | No additional stability data | SmPC |
| **Rituximab**[a] | **Mabthera 1400 mg/11.7 m solution for subcutaneous injection** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Rituximab | Rixathon 100 mg and 500 mg concentrate for solution for infusion | Sandoz | 7 days at ≤30 °C | No additional stability data | SmPC |
| Rocuronium | Esmeron 10 mg/ml solution for injection | Schering-Plow | 3 months at ≤25 °C | No additional stability data | SmPC |
| Romiplostim | Nplate 250 mcg, 250 mcg, and 500 mcg powder for solution for injection | Amgen | 30 days at ≤25 °C. | 10 days between 27 and 30 °C | Mateo *et al.* (2017) |
| **Rotavirus vaccine**[a] | **Rotateq oral solution vaccine** | **Merck** | **Keep at 2–8 °C** | **12 h at ≤25 °C** | **Manufacturer** |
| Rurioctocog alfa | Adynovi 250 IU/5 ml, 500 IU/5 ml, 1000 IU/5 ml, 2000 IU/5 ml, and 3000 IU/5 ml powder and solvent for solution for injection | Baxalta Innovations | 3 months at ≤30 °C | No additional stability data | SmPC |

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Sargramostim | Leukine 250 mcg powder for concentrate for solution for infusion | Pharma International | Keep at 2–8 °C | 12 months at ≤25 °C. 3 months at ≤40 °C | Manufacturer |
| Sarilumab | Kevzara a 150 mg and 200 mg solution for injection in pre-filled syringe/pen | Sanofi | 14 days at ≤25°C | No additional stability data | SmPC |
| Secukinumab | Cosentyx 75 mg and 150 mg solution for injection in pre-filled syringe | Novartis | 4 days at ≤30°C | No additional stability data | SmPC |
| Simoctocog alfa | Nuwiq 250 IU, 500 IU, 1000 IU, and 2000 IU powder and solvent for solution for injection | Octapharma AB | 1 month at ≤25 °C. Do not freeze again | No additional stability data | SmPC |
| Somatropin | Genotonorm Miniquick 0.2 mg, 0.4 mg, 0.6 mg, 0.8 mg, 1 mg, 1.4 mg, 1.6 mg, and 2 mg powder and solvent for solution for injection | Pfizer | 6 months at ≤25 °C. Do not freeze again | No additional stability data | SmPC |
| Somatropin | Omnitrope 1.3 mg/ml powder and solvent for solution for injection | Sandoz | Keep at 2–8 °C | 48 h at ≤25 °C | Manufacturer |
| Somatropin | Humatrope 6 mg, 12 mg, and 24 mg powder for solution for injection | Lilly | Keep at 2–8 °C | 28 days at ≤10 °C; 20 days at ≤15 °C; 11 days at ≤20 °C; 6 days at ≤25 °C; 4 days at ≤30 °C; 48 h at ≤35 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |
| Somatropin | Saizen 8 mg/ml and 5.83 mg/ml solution for injection in cartridge | Merck | 7 days at ≤25 °C | No additional stability data | SmPC |
| Temsirolimus | Torisel 30 mg concentrate and solvent for solution for infusion | Pfizer | Keep at 2–8 °C | 24 h at ≤25 °C | Mateo *et al.* (2017) |
| Teriparatide | Forsteo 20 µg/80 µl solution for injection in pre-filled pen | Lilly | Keep at 2–8 °C | 14 days at ≤10 °C; 7 days at ≤15 °C; 3.5 days at ≤20 °C; 48 h at ≤25 °C; 24 h at ≤30 °C; 14 h at ≤35 °C; 8 h at ≤40 °C | Mateo *et al.* (2017); Ardanaz (2008) |
| Tetanus immunoglobulin | 250 IU solution for injection in pre-filled syringe | Grifols | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Tetracosactide | Nuvacthen Depot 1 mg suspension for injection | Alfasigma | Keep at 2–8 °C | 24 h at ≤25 °C | Manufacturer |
| Tetrahidrocannabinol | Sativex 2.7 mg/2.5 mg solution in a spray | Almirall | No need to keep in the refrigerator (open) | 10 days at ≤25 °C | Mateo *et al.* (2017) |
| Tidlrakizumab | Ilumetri 100 mg and 200 mg solution for injection in pre-filled syringe | Almirall | 1 month for a single period at ≤25 °C | No additional stability data | SmPC |
| Tisagenlecleucel | Kymriah 1.2–600 million cells dispersion for infusion | Novartis | Once completely thawed, stored at room temperature (20–25 °C), it should be administered within 30 min. The product should not be refrozen once thawed | No additional stability data | SmPC |
| Tobramycin | inhalation solution 300 mg/5 ml | Teva Pharma | 28 days at ≤25 °C | No additional stability data | SmPC |
| Tocilizumab | Roactemra 162 mg solution for injection in pre-filled syringe | Roche | 14 days ≤30 °C | No additional stability data | SmPC |
| Trabectadine | Yondelis 0.25 mg and 1 mg powder for concentrate for solution for infusion | PharmaMar | Keep at 2–8 °C | 5 days at 25 °C ± 2 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |
| Tralokinumab | Adtralza 150 mg and 300 solution for injection in pre-filled syringe | Leo Pharma | 14 days ≤30 °C | No additional stability data | SmPC |
| Trastuzumab | Herceptin 150 mg powder for concentrate for solution for infusion | Roche | 6 h at ≤30 °C | No additional stability data | SmPC |
| **Trastuzumab emtansine**[a] | **Kadcyla 100 mg and 160 mg powder for concentrate for solution for infusion** | **Roche** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Turoctocog alfa | NovoEight 250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU, and 3000 IU powder and solvent for solution for injection | Novo Nordisk | 9 months for a single period at ≤30 °C and 3 months at ≤40 °C. Do not refrigerate again. | No additional stability data | SmPC |
| Ustekinumab | Stelara 130 mg concentrate for solution for infusion | Janssen | 8 h at ≤25 °C | No additional stability data | SmPC |
| Ustekinumab | Stelara 45 mg and 90 mg solution for injection in pre-filled syringe | Janssen | 1 month at ≤30 °C. Do not refrigerate again | No additional stability data | SmPC |
| Vedolizumab | Entyvio 300 mg powder for concentrate for solution for infusion | Takeda Pharmaceuticals International | Keep at 2–8 °C | 48 h at ≤25 °C. Do not freeze again | Mateo *et al.* (2017) |
| Vinblastine | Vinblastine Stada 10 mg powder for solution for injection | Stada | Keep at 2–8 °C | 1 month at ≤25 °C | Mateo *et al.* (2017) |
| **Vincristine**[a] | **Vincristine Pfizer 1 mg/ml solution for injection** | **Pfizer** | **Keep at 2–8 °C** | **24 h at ≤25 °C** | **Manufacturer** |
| Vindesine | Enison 5 mg powder for solution for injection | Stada | Keep at 2–8 °C | 21 days at ≤15 °C and 14 days at ≤25 °C | Ricote-Lobera *et al.* (2013) |
| Vinflunine | Javlor 25 mg/ml concentrate for solution for infusion | Pierre Fabre | Keep at 2–8 °C | 72 days at ≤30 °C | Mateo *et al.* (2017) |

(*continued on next page*)

**Table 1** (*continued*)

| Drug product | Brand name (Manufacturer) | Manufacturer | Storage information contained in SmPC | Additional stability data | Source of Information |
|---|---|---|---|---|---|
| Vinorebilne | 20 mg and 40 mg soft capsules | Glenmark Arzneimittel GMBH | Keep at 2–8 °C | 6 months at ≤27 °C | Manufacturer |
| Vinorelbine | Navelbine 10 mg/ml concentrate for solution for infusion | Pierre Fabre | Keep at 2–8 °C | 6 months at 25 ± 2 °C | Manufacturer |
| Voriconazole | Vfend 40 mg/ml powder for oral suspension | Pfizer | Keep at 2–8 °C | 1 month at ≤25 °C | Mateo *et al.* (2017); Ricote-Lobera *et al.* (2013) |

SmPC: Summary of product characteristics.
[a] Stability information only valid for a specific case of storage error. In case of irregularities in the cold chain, contact with the manufacturer is recommended.

sourced from published articles and gray literature: 36 (17.7%) from Mateo *et al.*,[11] 8 (3.9%) from Ricote-Lobera *et al.*,[12] 1 (0.49%), from Ardanaz *et al.*,[13] 1 (0.49%) from Bovaira *et al.*,[14] and 1 (0.49%) from Periáñez *et al.*, (2011)[2] and 9 (4.4%) from various references.

Finally, a total of 27 manufacturers were contacted to provide relevant information for the remaining 52 (25.6%) drugs. In 21 instances, the stability information was applicable only to specific cases of storage errors, characterized by distinct storage conditions and pertaining to specific batches of the product (these drugs are indicated in bold type in the table).

## Discussion

Our study demonstrates that the vast majority of drugs requiring refrigeration maintain adequate stability at room temperature for at least 24 h. In practice, most temperature excursions in hospital refrigeration systems (including pharmacy services and other clinical units or outpatient clinics) are identified before reaching 24 h. Therefore, our findings indicate that, in most cases, it is unnecessary to discard medications due to these excursions. Furthermore, a significant proportion of outpatient medications dispensed by hospital pharmacy services exhibit excellent stability at room temperature over extended periods. This is particularly relevant given that some studies reveal that less than 10% of patients manage to keep their thermolabile medications within the recommended temperature range of 2–8 °C throughout the entire duration of home storage,[6,15,16] while the medications included in our study account for one-third of the total. Additionally, temperature excursions for outpatient medications are typically detected less rapidly than in the hospital environment due to a lack of temperature control, monitoring systems, and alarms.

Similarly, the results of our study show that many storage errors reported by patients for various reasons (e.g., forgetfulness, malfunctioning refrigeration systems) do not necessarily require the affected medications to be discarded. The exponential increase in drug costs makes it increasingly important to optimize storage practices to mitigate costs associated with storage errors. In the case of thermolabile drugs, the financial implications of a storage error are generally greater than in other cases, as many of the higher-cost drug categories require refrigeration (e.g., monoclonal antibodies, biological drugs).

Notably, in 40.3% of the inquiries made, manufacturers indicated that the stability information provided was applicable only to specific cases of storage errors, which were characterized by unique storage conditions and specific batches of the product. In such instances, manufacturers recommended contacting them if any irregularities were detected in the maintenance of the cold chain. This percentage aligns with findings from other studies.[12]

Several studies have been published on this topic,[3,7–13] generally employing methodologies similar to ours. Most of these studies include information about thermolabile drugs listed in the hospital's pharmacotherapeutic guide. To obtain this information, non-systematic reviews were conducted, utilizing similar sources. The results were also presented in a comparable format. Thus, the primary contribution of our study lies in its compilation and update of all existing information on this subject, providing data for a greater number of medications than previous works.

Considering these factors, our study can serve as a valuable resource for healthcare professionals responsible for medication storage at the hospital level, enabling quick consultation regarding the maximum stability of the majority of drugs currently used in the hospital environment and/or dispensed by hospital pharmacy units. This information, which is often difficult to locate, represents the most up-to-date and comprehensive study of its kind published to date. Without exposing patients to any risk, our results table can help prevent unnecessary drug loss and minimize time wasted due to inappropriate storage temperatures.

One limitation of our study is that we did not conduct a systematic review of the literature, which may have resulted in the omission of some stability data. However, the published literature on this issue is limited, and the information available constitutes only a portion of our study. Furthermore, this type of information is often found in gray literature, which is more challenging to access compared to that published in scientific journals. We also did not perform a systematic search for this type of literature, so information contained in those sources may have been overlooked. Additionally, our study did not present information in languages other than English or Spanish. Another limitation is that we only collected data from the pharmacotherapeutic guide of our hospital.

It is also important to emphasize that in some cases, the information provided by manufacturers was applicable only to specific instances of temperature excursions involving particular batches of the drug. Consequently, this information may not be fully extrapolated to other cases of temperature excursions. Therefore, we recommend consulting the manufacturer regarding the viability of affected batches.

As noted by other authors, it is necessary for pharmaceutical manufacturers to publish the results of stability studies conducted outside the recommended storage conditions specified in the SmPC to facilitate access to this critical information, even if accompanied by a disclaimer indicating that the data should be considered indicative only.

The number and cost of thermolabile drugs have increased exponentially in recent years. The majority of these drugs maintain adequate stability at room temperature for limited periods, with some exhibiting stability for longer durations. To date, our study presents stability data for the largest number of drugs. Therefore, the results of our study constitute a highly valuable and updated tool for saving time and resources in hospital pharmacy units. It is essential for pharmaceutical manufacturers to publish the results of stability studies conducted outside the recommended storage conditions in the SmPC.

## Contribution to evidence

In our study, we summarize the existing evidence published to date regarding the storage of thermolabile drugs. Additionally, we update this information and augment it with new stability data for various medications. To our knowledge, this is the largest published work on this issue worldwide and represents a modest yet valuable contribution to the clinical practice of hospital pharmacists.

The results of our study are presented in a tabular format, serving as a highly useful and up-to-date resource for saving time and reducing costs in hospital pharmacy units.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Ethical considerations

Not applicable to the present work.

## Declaration of authorship

Conception and design of this work: Hector Acosta García, Paloma Suarez Casillas and Santiago José Lora Escobar.

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## CRediT authorship contribution statement

**Paloma Suárez-Casillas:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Santiago José Lora-Escobar:** Writing – original draft, Formal analysis, Data curation. **Elena Montecatine-Alonso:** Writing – review & editing, Conceptualization. **Tao Li:** Formal analysis, Data curation. **Hector Acosta-García:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Conceptualization.

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