



1 May 2020

Medicine Supply Alert Notice

Ativan® (lorazepam) 4mg/mL Solution for injection

Priority: Level 3*

Valid until: 19 June 2020

Issue

1. Ativan® (lorazepam) 4mg/mL solution for injection will be out of stock from w/c 27th April until w/c 15th June 2020.
2. The US product, lorazepam injection 2mg/mL, supplied in Carpuject™ single dose cartridges will be available to Boards from early May 2020 on an 'unlicensed' basis.
3. Carpuject™ single dose cartridges can be considered bioequivalent to the UK brand Ativan® (lorazepam) 4mg/mL solution for injection and no dosing adjustments should be required.
4. Carpuject™ cartridges must be used in combination with the Carpuject™ holder provided. Injection in cartridge is diluted with an equal volume of compatible solution for IV administration (IM injection is administered undiluted). More information on Carpuject™ single dose cartridges can be found in **Annex A**.
5. Ativan® (lorazepam) 4mg/mL solution for injection supplies will remain available for primary care customers throughout this period (see ordering information below).

Advice and Actions

6. All healthcare organisations in secondary or specialist healthcare services should work with clinicians including pharmacists to ensure the following actions are undertaken where relevant.
 - i. Prioritise remaining supplies of lorazepam 4mg/mL solution for injection for indications where alternatives are not appropriate.
 - ii. Consider prescribing the unlicensed US product, lorazepam injection 2mg/mL supplied in Carpuject™ single dose cartridges.
 - iii. Although Carpuject™ single dose cartridges can be considered bioequivalent to the UK brand Ativan® (lorazepam) 4mg/mL solution for injection and no dosing adjustments should be required, **there are significant differences in method of administration and also in solution strength which staff need to be made aware of and appropriately trained in.**
 - iv. Use the resources provided (links below and/or attached) to ensure staff administering lorazepam injection 2mg/mL single dose cartridges are familiar with the method of dilution and administration.
 - v. Ensure support through your Board's Medicines Governance arrangements to ensure safe introduction of the lorazepam injection 2mg/mL single dose cartridges and dedicated Carpuject™ holder.
 - vi. If lorazepam injection 2mg/mL in single dose cartridges are not considered suitable or Boards are unable to obtain a sufficient quantity to meet their local requirements, then clinicians should consider alternative medications to lorazepam during this time (see further advice below).

7. Any decision to prescribe an unlicensed medicine should consider the relevant guidance about unlicensed medicines and NHS Board or local governance procedures. Please see the links below for further information:
- [Prescribing unlicensed medicines](#), General Medical Council (GMC)
 - [The supply of unlicensed medicinal products](#), Medicines and Healthcare products Regulatory Agency (MHRA)
 - [Professional Guidance for the Procurement and Supply of Specials](#), Royal Pharmaceutical Society (RPS)
8. When prescribing and dispensing unlicensed preparations, prescribers and pharmacists should always ensure that patient consent has been sought for use of an unlicensed preparation.

Additional Information

Ordering information

9. Lorazepam injection 2mg/mL single dose cartridges can be ordered through the new PIP code **8140907** via Alliance Healthcare. EAN Code is **(01)10304091985305**.
10. Allocations of **30 packs/calendar month per Board** have been implemented to ensure supplies of the unlicensed product remain available throughout the affected period. Customers who reach this cap can contact Pfizer's Customer Contact Centre directly on 0845 608 8866 to request further supplies.
11. Pfizer have confirmed they will retain sufficient stock of Ativan® (lorazepam) 4mg/mL solution for injection to ensure ongoing supplies remain available for community pharmacies throughout this period. Supplies for community pharmacy accounts should continue to be ordered via Alliance Healthcare using PIP code **8019127**. EAN Code is **5391521021205**. For any queries on stock ordering please contact the Pfizer Customer Contact Centre on 0845 608 8866.

Alternative unlicensed imports

12. The following importer companies currently have stock of unlicensed lorazepam 4mg/mL injection or can source limited supplies; however, the average lead time is **4-6 weeks** (please note there may be other companies that can also source supplies):
- Clinigen
 - Mawdsleys

Alternative treatment options

13. The UKMi memo (link below) provides further information on potential alternative agents that might be considered if the unlicensed lorazepam injection options (Carpurject™ and other unlicensed imports) are not deemed appropriate or are insufficient to meet local requirements. <https://www.sps.nhs.uk/articles/shortgae-of-ativan-lorazepam-injection-4-mg-in-1-ml/>
- In all cases, expert advice should be sought on choice of an alternative agent and healthcare professionals are encouraged to agree treatment approaches with their pharmacy teams once supply of alternatives has been confirmed. During this period there are also limited supplies of some of the alternative agents to lorazepam including diazepam 10mg/2mL emulsion for injection (Diazemuls®), which is currently long term out of stock until at least October 2020 (see MSAN (2020)22).

Enquiries

14. Enquiries from Health Boards or healthcare professionals should be directed in the first instance to PharmacyTeam@gov.scot (primary care) or NSS.NHSSMedicineShortages@nhs.net (secondary care).

Lorazepam injection 2mg/ml in Carpuject™ single dose cartridges

To help mitigate the shortage, Pfizer have sourced lorazepam injection 2mg/ml in Carpuject™ single dose cartridges from the US, which are considered unlicensed in the UK.



Figure 1. Lorazepam injection 2mg/ml in Carpuject single dose cartridge

Figure 2. Carpuject holder

This product can be considered bioequivalent to Ativan® 4mg/mL injection and therefore no dosing adjustments should be required (**note difference in solution strength**).

However, due to differences in presentation between the UK and US products, pharmacy departments should work closely with their local Medicines Governance arrangements when introducing this medication.

Links to useful resources can be located below and can also be found along with a user guide in **Annex B** and unlicensed medicine quality assessment at https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=103548.

Product monographs

UK Summary of Product Characteristics and Patient Information Leaflet for Ativan® 4mg/mL Solution for Injection (lorazepam): <https://www.medicines.org.uk/emc/product/5473>

US Summary of Product Characteristics and Patient Information Leaflet for lorazepam injection 2mg/mL (note that this is a link to the information referenced in the 'Summary of product characteristics' of the Unlicensed Medicine Quality Assessment which has been shared with this alert): <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=20140b19-846b-425f-b191-670e17809945>

Training video

Instructions on the use of the Carpuject™ cartridges and holder: <https://www.pfizerpro.com/product/readytouse> (video).

Orders for lorazepam injection 2mg/mL single dose cartridges will be provided with compatible Carpuject™ holders. Whilst the holders are designed to be reusable, Pfizer will be supplying enough holders with each order to enable them to be used once only then discarded. Lorazepam injection 2mg/mL single dose cartridges must be used in combination with the Carpuject™ holder for dilution/administration of the solution.

The solution must **not** be withdrawn directly from the cartridge.

Key differences between Ativan® 4mg/mL solution for Injection

Product Name	Lorazepam injection, solution 2mg/ml	Ativan® 4mg/ml Solution for Injection (lorazepam)
Distributed by	Hospira Inc USA	Pfizer Ltd UK
Licensed Indication	Status Epilepticus Preanesthetic medication	Status epilepticus. Pre-operative medication or premedication Treatment of acute anxiety states, acute excitement or acute mania.
Solution strength/dose	Each cartridge contains 2mg (1ml of 2mg/ml solution)	Each ampoule contains 4mg (1ml of 4mg/ml solution)
Primary Container	Carpject™, Single-dose cartridge with Luer Lock for the Carpject™ Syringe System	Ampoule (type I glass) with a one-point-cut opening
Pack size	10 cartridges of 1ml solution for injection	10 ampoules of 1ml solution for injection
Administration	Carpject™ cartridges must be used in combination with the Carpject™ holder provided. Injection in cartridge is diluted with an equal volume of compatible solution for IV administration (IM injection is administered undiluted)	Contents of ampoule diluted with saline or sterile water for injection BP as a 1:1 dilution for IV administration. (may also be diluted for IM administration)

List No. 2049-02 Rx only GTIN: 10304092049020

CL12

CARPUJECT™ Syringe System

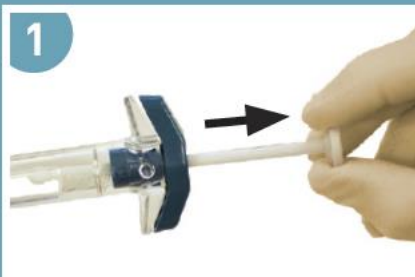


Optional Assisted Method for Opening SLIM-PAK™ Package

1. Slide the square opening on the holder over the tip of the SLIM-PAK cap.
2. Hold the SLIM-PAK stationary while turning the holder to break the tamper evident seal and open the SLIM-PAK.



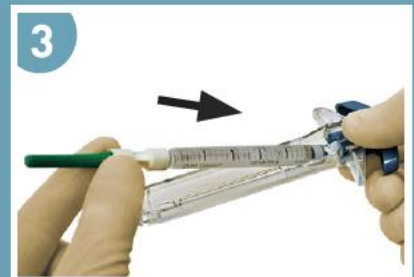
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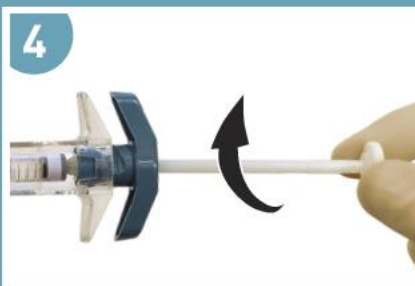
Grasp the holder with the open side facing you and pull the white plunger rod back until it clicks.



Turn the blue handle to the left (Counterclockwise) 180° until it clicks.



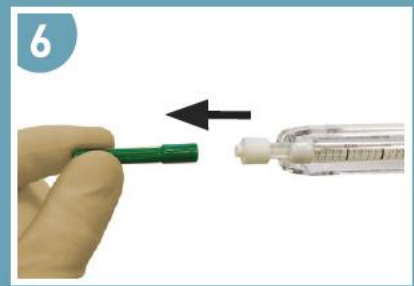
Insert the cartridge in the holder by placing the end with the plunger in the holder first and ensure the cartridge lays flat.



Screw the white plunger rod onto the plunger until you feel a slight resistance.



Turn the blue handle to the right (Clockwise) 180° until it clicks. **Note:** This step creates an open fluid pathway; therefore the drug must be used or discarded after this step.



Remove and discard green luer cap. Do not touch the luer end of the syringe. Expel air as needed. Administer prescribed dose.