



UPDATE:

Update to communication issued 6 October 2020

Medicine Supply Notification

MSN/2020/054-U

Ativan[®] (lorazepam) 4mg/ml Solution for injection (Pfizer)

Tier 2- medium impact*

Date of issue: 2 December 2020

Summary

- Ativan[®] (lorazepam) 4mg/ml solution for injection continues to be out of stock, with no confirmed date of resupply; remaining stock will continue to be reserved for primary care only (see ordering information below).
- Pfizer have sourced an alternative product from Canada, LORAZEPAM injection USP, sterile solution 4mg/ml in multi-dose glass vials. The constituents/excipients of UK and Canadian formulations are essentially identical as are their respective licensed indications. A more detailed comparison is available in the Supporting Information section below and in Pfizer's Dear Health Care Professional (HCP) letter and the quality assessment document, attached to this communication.
- Canadian lorazepam injection USP, sterile solution 4mg/ml vials will be available for order during the course of week commencing 7th December and subject to a weekly allocation limit per organisation to ensure equity of supply (see ordering information below).
- The US lorazepam injection 2mg/ml, supplied in Carpuject[™] single dose cartridges with the Carpuject[™] holder, which have been covering the Ativan[®] shortage since October, will cease to be available to order during the course of week commencing 7th December.
- Importer companies have indicated they can source supplies of non-UK licensed lorazepam, availability, strength and lead times vary.

Actions Required

Trust pharmacy procurement teams and clinical leads should work with the local Medication Safety Officer (MSO) to ensure the following actions are undertaken where relevant:

- i. consider prescribing the non-UK licensed Canadian product, lorazepam USP, sterile solution 4mg/ml. The Canadian product is the same concentration as UK licensed Ativan[®] and is considered similar in terms of presentation (see supporting information, the attached Dear HCP letter and national QA document) and place orders weekly;
- ii. where Trusts have previously switched to Carpuject[™] engage with MSO to:

*Classification of Tiers can be found at the following link: [A Guide to Managing Medicines Supply and Shortages.](#)

- ensure all affected clinical areas are aware of this shortage and have a plan in place for the management of the switch over from US Carpuject™ lorazepam 2mg/ml single dose cartridges to Canadian, lorazepam injection USP, sterile solution 4mg/ml vials;
 - ensure clinical colleagues are made aware of the significant differences in method of administration and also in solution strength between the US and Canadian products;
- iii. if Canadian product, lorazepam USP, sterile solution 4mg/ml is not considered suitable or Trusts are unable to obtain a sufficient quantity to meet their local requirements they should consider:
- placing orders for non-UK licensed lorazepam; and/or
 - using alternative medications as outlined in the “Alternative agents and management options” section below; and
- iv. if Trusts are likely to have multiple unlicensed products in use within the organisation at the same time consideration is given and mitigations put in place to minimise the risk of product confusion and dosing errors.

Supporting Information

Lorazepam injection USP, sterile solution 4mg/ml glass vials

To help mitigate the shortage, Pfizer have sourced lorazepam injection 4mg/ml glass vials from Canada, which are considered unlicensed in the UK.



Figure 1. Lorazepam injection USP 4mg/ml multidose glass vials, outer packaging

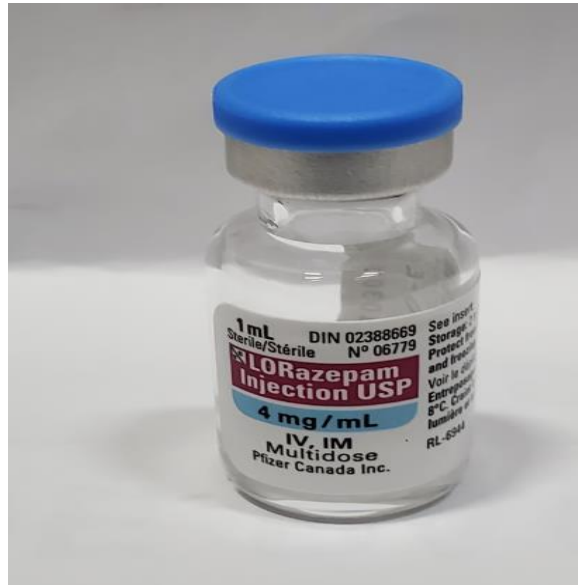


Figure 2. Lorazepam injection USP 4mg/ml multidose glass vial

This product can be considered bioequivalent to lorazepam (Ativan®) 4mg/ml injection and therefore no dosing adjustments should be required. Although the Canadian product is supplied in a multi-dose vial it is expected that the vial should be for single dose use as per existing practice with the Ativan® ampoules.

North West Pharmaceutical Quality Assurance, on behalf of SPS, has performed a national quality assessment, this is included as an attachment to this MSN communication and contains further information including the Canadian product monograph and patient information leaflet for lorazepam USP.

Pfizer UK has prepared a Dear HCP letter, approved by the MHRA, which is included as an attachment to this MSN and will also be sent out alongside each order for the Canadian product. The table below outlines the main differences between UK lorazepam (Ativan®) 4mg/ml injection and the Canadian lorazepam injection 4mg/ml glass vials.

Key differences between lorazepam (Ativan®) 4mg/ml Solution for Injection and lorazepam injection USP 4mg/ml multidose glass vials

Marketing Authorisation Holder	Pfizer Canada ULC,	Pfizer Limited (UK)	Hospira Inc USA
Product Name	LORAZEPAM injection USP, sterile solution 4mg/ml	Ativan 4mg/ml Solution for Injection (Lorazepam)	Lorazepam injection, solution 2mg/ml
Licensed Indication	Anxiety: Lorazepam Injection USP is useful for the short-term relief of manifestations of severe anxiety in people with anxiety neurosis. It is also useful for the relief of excessive anxiety that might be present prior to surgical interventions. Status epilepticus: Lorazepam Injection USP is useful to help control severe seizures	Pre-operative medication or premedication for uncomfortable or prolonged investigations, e.g. bronchoscopy, arteriography, endoscopy. The treatment of acute anxiety states, acute excitement or acute mania. The control of status epilepticus.	Status Epilepticus Preanesthetic medication
Solution strength/dose	Each vial contains 1ml of 4mg/ml solution for a full dose of 4mg	Each ampoule contains 1ml of 4mg/ml solution for a full dose of 4mg	Each cartridge contains 2mg (1ml of 2mg/ml solution)
Primary Container	Multi-dose glass vials with latex-free stoppers	2ml ampoules (Type I glass) with a one-point-cut opening	Carpject™, Single-dose cartridge with Luer Lock for the Carpject™ Syringe System
No. of Packs	10 vials of 1ml; Each vial contains 1ml of solution for injection	10 ampoules of 1ml; Each ampoule contains 1ml of solution for injection	10 cartridges of 1ml solution for injection
Administration	When given intramuscularly, Lorazepam Injection USP, undiluted, should be injected deep into a muscle mass. Immediately prior to intravenous use, Lorazepam Injection USP must be diluted with an equal volume of compatible solution. When properly diluted the drug may be injected directly into a vein or into the tubing of an existing intravenous infusion. The rate of injection should not exceed 2 mg/minute. Refer to the Canadian Summary of Product Characteristics for full administration guidance and solution compatibilities.	Ativan Injection can be given intravenously or intramuscularly. However, the intravenous route is to be preferred. Care should be taken to avoid injection into small veins and intra-arterial injection. Intramuscular administration: A 1:1 dilution of Ativan Injection with normal saline or Sterile Water for Injection BP is recommended in order to facilitate intramuscular administration. Intravenous administration: For intravenous administration, Ativan Injection should always be diluted with saline or Sterile Water for Injection BP as a 1:1 dilution. Ativan Injection is presented as a 1ml solution in a 2ml ampoule to facilitate dilution. Refer to the UK Summary of Product Characteristics for full administration guidance and solution compatibilities.	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)

Ordering Information

Canadian lorazepam USP injection 4mg/ml glass vials can be ordered through Pfizer's Customer Contact Centre directly on **0845 608 8866**, PIP code **8025132**. The expiry date of the product is July 1st, 2021.

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Allocations of 5 packs per week per Trust have been implemented to ensure supplies of the unlicensed product remain available throughout the affected period. Trusts that reach this cap and have urgent medical need can contact Pfizer's Customer Contact Centre who will be able to assist. This allocation cap will be reviewed regularly.

Pfizer have confirmed they will retain all remaining stock of lorazepam (Ativan®) 4mg/ml solution for injection to preserve supplies for community pharmacies for as long as possible. 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 agents and management options

Alternative unlicensed imports

The following importer companies currently have stock of non-UK licensed lorazepam, 4mg/ml and/or 2mg/ml, injection or have indicated they can source supplies:

- Clinigen;
- Durbin PLC;
- Mawdsleys Unlicensed;
- Target Healthcare; and
- Waymade PLC

However, quantities available and lead times vary so please contact the companies directly for up to date information. Please note there may be other companies that can also source supplies and that this information is correct at time of issue but is subject to change.

Any decision to prescribe an unlicensed medicine must consider the relevant guidance and NHS Trust 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); and
- [Professional guidance for the procurement and supply of specials](#), Royal Pharmaceutical Society (RPS).

Alternative treatment options

The UKMi [memo](#) provides further information on potential alternative agents that might be considered if the unlicensed lorazepam injection options are not deemed appropriate or are insufficient to meet local requirements.

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 February 2021.

Please note - with regards to use of midazolam injection, Trusts should ensure compliance with the [NPSA alert](#) on reducing the risk of overdose with this preparation.

Enquiries

Enquiries from NHS Trusts in England should in the first instance be directed to your Regional Pharmacy Procurement Specialist, who will escalate to national teams if required.

REGION	Full Name	Email
East Midlands	Andi Swain	andi.swain@nhs.net
East of England	James Kent	james.kent@southend.nhs.uk
London	Jackie Eastwood	jacqueline.eastwood@lpp.nhs.uk
North East	David Cook	david.cook20@nhs.net
North West	Glenn Harley	Glenn.Harley@liverpoolft.nhs.uk
South Central	Alison Ashman	Alison.Ashman@berkshire.nhs.uk
South East Coast	Richard Bateman	richard.bateman2@nhs.net
South West	Danny Palmer	Danny.Palmer@UHBristol.nhs.uk
West Midlands	Diptyka Hart	Diptyka.Hart@uhb.nhs.uk
Yorkshire & Humber	David Allwood	davidallwood@nhs.net

Scotland

nss.nhssmedicineshortages@nhs.scot

Wales

MedicinesShortages@gov.wales

Northern Ireland

Noel.dunn@northerntrust.hscni.net

All other organisations should send enquiries about this notice to the DHSC Medicine Supply Team quoting reference number MSN/2020/054-U.

Email: DHSCmedicinesupplyteam@dhsc.gov.uk

Communication prepared by pharmacy team at the Commercial Medicines Unit, NHS England & NHS Improvement