Department of Health & Social Care

NHS

Supply Disruption Alert

SDA/2020/006 Issued: 28 April 2020 Valid until: 19/06/2020

Ativan® (lorazepam) 4mg/ml Solution for injection – Supply Disruption

Summary

- Ativan® (lorazepam) 4mg/ml solution for injection will be out of stock from w/c 27th April until w/c 15th June 2020.
- The US product, lorazepam injection 2mg/ml, supplied in Carpuject™ single dose cartridges will be available to Trusts from early May 2020 on an 'unlicensed' basis.
- 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.
- 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).
- Ativan® (lorazepam) 4mg/ml solution for injection supplies will remain available for primary care customers throughout this period (see ordering information below).

Action

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 gained from your Medication Safety Officer 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 Trusts 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).

Any decision to prescribe an unlicensed medicine should consider the relevant guidance about unlicensed medicines 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)
- Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS)

When prescribing and dispensing unlicensed preparations, prescribers and pharmacists should always ensure that patient consent has been sought for use of an unlicensed preparation.

Deadlines for actions

Actions underway:	30/04/2020
Actions completed:	19/06/2020

Product details

Pfizer Ativan® (lorazepam) 4mg/ml Solution for injection 10 x 1ml

Problem / background

There is a short-term supply issue affecting Ativan® injection caused by a manufacturing delay of UK licensed stock due to COVID-19. Pfizer are the sole licensed UK supplier of lorazepam 4mg/ml solution for injection.

It is anticipated that current stock will be depleted week commencing 27th April 2020. Further deliveries are currently anticipated w/c 15th June 2020.

Ativan® injection is licensed for pre-operative medication or premedication for uncomfortable or prolonged investigations, the treatment of acute anxiety states, acute excitement or acute mania and the control of status epilepticus.

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 Safety Officers (MSO) when introducing this medication.

Links to useful resources can be located below and can also be found along with a user guide and unlicensed medicine quality assessment with this alert on the CAS website.

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 and lorazepam injection 2mg/ml single use cartridges

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	Carpuject™, Single-dose cartridge with Luer Lock for the Carpuject™ 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	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)	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)

Ordering Information

Lorazepam injection 2mg/ml single dose cartridges can be ordered through the new PIP code **8140907** via Alliance Healthcare. EAN Code is **(01)10304091985305.**

Allocations of 30 packs/calendar month per Trust 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.

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 agents and management options

Alternative unlicensed imports

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

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.

Distribution

Trusts (NHS boards in Scotland and Wales)

CAS and SABS (NI) liaison officers for onward distribution to all relevant staff including:

- A&E consultants
- A&E departments
- A&E directors
- A&E nurses
- Adult intensive care units
- Anaesthesia, directors of
- Anaesthetic medical staff
- Anaesthetic nursing staff
- Anaesthetists
- Chief pharmacists
- Clinical governance leads
- Clinical Procurement Specialists
- District nurses
- Hospital at home units
- Hospital pharmacies
- Hospital pharmacists
- Intensive care medical staff/paediatrics
- Intensive care nursing staff (adult)
- Intensive care nursing staff (paediatric)
- Intensive care units
- Intensive care, directors of
- IV nurse specialists
- Intensive care, directors of
- Mental health teams
- Mental health nursing staff (adult)
- Mental health nursing staff (paediatric)

- Paediatric intensive care units
- Palliative care teams
- Pharmaceutical advisors
- Pharmacists
- Paediatric medicine, directors of
- Purchasing managers
- Theatre managers
- Theatre nurses

NHS England Regional Offices
CAS liaison officers for onward distribution to all relevant staff including:
- Community pharmacists

General Practice
For onward distribution to all relevant staff including:
- General practitioners
- General practice managers
- General practice nurses

Independent distribution

Establishments registered with the Care Quality Commission (CQC) (England only)
- Care homes providing nursing care (adults)
- Clinics
- Domiciliary care providers
- Hospices
- Hospitals in the independent sector
- Independent treatment centres
- Nursing agencies
- Private medical practitioners

Enquiries

Enquiries from NHS Trusts in England should in the first instance be directed to your trust pharmacy team who will escalate issues to the Regional Pharmacy Procurement Specialist and 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.Cook@nth.nhs.uk
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.net

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 **SDA/2020/006**

Email: supplyresiliencemd@dhsc.gov.uk