NSW Health

UPDATED Disruption to supply – Azithromycin (Zithromax) 200 mg/5 mL powder for oral suspension

SAFETY NOTICE 025/24

Issue date:	19 September 2024
Replaces:	SN:010/24
Content reviewed by:	Medication Safety Expert Advisory Committee (MSEAC) Medication Shortage Assessment Management Team (MSAM)
Distributed to:	Chief Executives; Directors of Clinical Governance; Director, Regulation and Compliance Unit
KEY MESSAGE:	NSW Health facilities are informed of the disruption to the supply of azithromycin 200 mg/5 mL powder for oral suspension, availability of international alternatives and associated safety considerations.
ACTION REQUIRED BY:	Clinicians
REQUIRED ACTION:	1. Distribute this Safety Notice to all relevant clinicians and clinical departments where azithromycin 200 mg/5 mL powder for oral suspension is held, prescribed, and administered, and include this Safety Notice in relevant handovers and safety huddles. 2. Undertake a local risk assessment and incorporate the below recommendations to manage the disruption to supply. 3. Ensure a system is in place to document actions taken in response to this Safety Notice. 4. Report any incidents associated with this disruption to supply into the local incident management system e.g., ims+. 5. Confirm receipt and distribution of this Safety Notice within **72 hours** to: CEC-MedicationSafety@health.nsw.gov.au.
DEADLINE:	COB 25 September 2024
We recommend you also inform:	Directors, Managers and Staff of: • Infectious Disease and Microbiology • Pharmacy • Nursing/Midwifery • Medical Services • Drug and Therapeutics Committees • Respiratory, Paediatric and Emergency Departments All other relevant clinicians, departments and committees.
Website:	https://www.health.nsw.gov.au/sabs/Pages/default.aspx http://internal.health.nsw.gov.au/quality/sabs/index.html
Review date:	March 2025

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What is updated in this Safety notice from SN:010/24?

This Safety Notice replaces SN:010/24 *Disruption to supply – Azithromycin 200 mg/5 mL powder for oral suspension* which has now been rescinded. The Safety Notice has been updated to include information on the availability of an additional international alternative azithromycin 200 mg/5 mL powder for oral suspension product under Section 19A of the *Therapeutic Goods Act 1989* (Pfizer brand from South Korea) and associated safety considerations. Additionally, since publication of the previous Safety Notice the Zydus branded international alternative from the USA has also been approved for supply under Section 19A (previously available under the Special Access Scheme).

Situation

There is an ongoing disruption to the supply of the Australian registered medicine azithromycin (Zithromax) 200 mg/5 mL powder for oral suspension (ARTG: 60049) due to unexpected increases in consumer demand until 31 January 2025. The disruption to supply coincides with an increase in the number of *Mycoplasma pneumoniae* infections in NSW. The increase in cases has also impacted the supply of other macrolide antimicrobials, such as clarithromycin (Klacid) 250 mg/5 mL powder for oral liquid.

At the time of publication, supply of alternative formulations of azithromycin, including 500 mg oral tablets and powder for intravenous infusion, remain unaffected. International alternatives of azithromycin powder for oral suspension are available under Section 19A (S19A) of the *Therapeutic Goods Act 1989*. NSW Health staff are advised to check the TGA website for updates regarding further changes to supply and the TGA S19A approvals database for updates on potential S19A alternatives.

Background

Azithromycin is a macrolide antimicrobial used to treat and prevent infections caused by susceptible bacteria including, but not limited to *Mycoplasma pneumoniae*, *Mycobacterium avium complex* (MAC), and *Bordetella pertussis*.

Azithromycin powder for oral suspension is used in paediatric patients and patients with enteral feeding tubes or swallowing difficulties. It is listed on the NSW Medicines Formulary with a restriction for use in accordance with the local antimicrobial stewardship policy.

Assessment

International alternatives have been approved for use under S19A of the *Therapeutic Goods Act 1989:*

- Azithromycin (Pfizer) powder for oral suspension from South Korea until 30 June 2025 via Pfizer.
- Azithromycin (Zydus) powder for oral suspension from the USA until 31 October 2024 via Medsurge.

The international alternatives differ to the Australian registered product in presentation, final volume, storage requirements, shelf life when reconstituted and excipients (see **Table 1** for comparison).

The Pfizer branded S19A alternative is not labelled in English and has been over-labelled with English instructions (see **Figure 1**). The product also contains a Korean Consumer Medicines Information (CMI) leaflet, which should be discarded and replaced with a copy of the Australian CMI.

Supply of azithromycin 200 mg/5 mL powder for oral suspension should be prioritised for paediatric populations and patients where alternative azithromycin formulations are not suitable. International alternatives may be considered for these patients if the Australian registered product is unavailable. In

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case of a complete disruption to supply of the powder for oral suspension, and alternative formulations of azithromycin are inappropriate, an alternative antibiotic will need to be used.

Figure 1: Pfizer South Korea S19A alternative front and back prior to over label being affixed (left) and with over labelling affixed (right).

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Recommendations

- Assess the current status and availability of azithromycin 200 mg/5 mL powder for oral suspension in each facility, ensuring all locations of stock are identified.
- Limit supply of azithromycin 200 mg/5 mL powder for oral suspension available in clinical areas (on 'imprest') while ensuring availability outside pharmacy operating hours.
- Ensure back orders based on average usage are placed with preferred wholesalers/suppliers for adequate distribution of stock when it becomes available.
- Reserve remaining supply of azithromycin 200 mg/5 mL powder for oral suspension for use when crushed oral tablet formulations are not suitable, for example:
    - patients requiring a non-solid oral dosage form where the prescribed dose is **not equivalent** to a full or half (scored formulations only) tablet – for example, **paediatric patients**
    - discharge supply.
- If international alternatives are used, consider important information provided in **Table 1**.
- Reserve supply of the Australian registered azithromycin (Zithromax) and the Pfizer branded S19A alternative powder for oral suspension products for patients under 6 months of age.
- If using the Pfizer branded S19A product from South Korea ensure:
    - measurements for reconstitution are performed with approved calibrated measuring cylinders as opposed to the measuring cup provided within the package
    - that two dispensing labels are affixed at the time of dispensing - one on the bottle (primary container) and one on the outer carton
    - a copy of the relevant Zithromax Australian CMI leaflet is provided and the Korean leaflet is discarded
    - all doses for administration are measured and administered using an oral syringe as opposed to the provided measuring spoon within the package
    - the expiry date is clearly indicated on the dispensing label (**5 days** after reconstitution).
- Crushed tablets should be used for doses equivalent to a full or half (scored formulations only) tablet be used when a non-solid oral dosage formulation of azithromycin is required, unless clinically unsuitable.
    - A mask and gloves should be worn when crushing the tablets (see SHPA Don't Rush to Crush, accessible via CIAP for further information).
    - Where crushed tablets are intended, this should be clearly specified on the medication order. For example, as an 'order comment' on the electronic Medication Management (eMM) system.
- Ensure that a suitable quantity is dispensed to the patient considering clinical indication and duration of treatment.
- Regularly review prescriptions for azithromycin for oral suspension and assess ongoing need for use.
- In case of a complete disruption to the supply, clinicians should carefully consider individual patient factors, condition being treated, and microorganism being targeted when selecting an alternative agent. Expert advice should be sought from Infectious Diseases/Microbiology if required.
- Establish regular liaison between Microbiology and Pharmacy Departments to discuss local stock situation and to help inform antibiotic susceptibility testing and reporting.

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Table 1. Comparison between Australian registered azithromycin 200 mg/5 mL and S19A alternatives.

	ARTG listed product	S19A alternative	
	Azithromycin **(Zithromax)** powder for oral suspension	Azithromycin **(Pfizer)** powder for oral suspension	Azithromycin **(Zydus)** powder for oral suspension
Country of registration	Australia	South Korea	USA
Supplier(s)	Pfizer	Pfizer	Medsurge
Active ingredient	Azithromycin dihydrate	Azithromycin dihydrate	Azithromycin dihydrate
Final concentration	200 mg/5 mL	200 mg/5 mL	200 mg/5 mL
Reconstituted volume	15 mL	15 mL	**30 mL**
Specific patient considerations	Not specified. Australian guidance supports use from birth.	Not specified	As per US Product Information: *Safety and effectiveness in the treatment of patients under 6 months of age have not been established.*
Excipients	• Sucrose • Tribasic sodium phosphate • Hyprolose • Xanthan gum • Spray dried artificial cher[illegible] No 24[illegible] • Spray dried artificial banana 15223 (ARTG PI No 246[illegible]) Crema vaniglia N 11489 Polvere SC613737 AR (ARTG PI No 117797)	• [illegible] • Sodium phosphate tribasic anhydrous • Hydroxypropyl cellulose • Xanthan gum • Artificial banana flavour • Artificial creme de vanilla flavour • Artificial cherry flavour	• Sucrose • Trisodium phosphate anhydrous • Hydroxypropyl cellulose • Xanthan gum • FD&C Red No. 40 • Cherry flavour • Ripe banana flavour
Labelling	English	Korean – over labelled with English as per TGA requirement	English
Storage requirements *Dry powder* *Reconstituted suspension* *Shelf life (reconstituted)*	 Below 30°C Below 30°C Use within 10 days	 In a tight container at room temperature Below 30 °C Use within **5 days**	 20 – 25°C 5 – 30°C Use within 10 days
Lead time	Refer to wholesaler and supplier portals	Contact suppliers for further information on availability and lead times (noting that lead times are variable and can be lengthy).	
Product image		TGA S19A information	TGA S19A Information

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